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IN MEMORIAM

HOLGER WERFEL SCHEUERMANN, Copenhagen

12 February 1877—2 March 1960

No more than a few months after an honorary doctorate had been conferred upon him by the University of Copenhagen in November 1959, H. W. Scheuermann passed away at the age of eighty-three.

Holger Scheuermann was the son of a general practitioner in Hørsholm. He took his degree in medicine in 1902 and became a specialist in orthopaedics and roentgenology in 1915. He was for a number of years director of the roentgen department of the Military Hospital and from 1936 of the Sundby Hospital, Copenhagen, until he retired in 1947. He continued in private practice as a radiologist at his home in Copenhagen up to a few years ago.

It was his description of the roentgenologic changes in juvenile dorsal kyphosis that made him famous. This was one of several papers on orthopaedic subjects which he wrote while working at the Copenhagen Home for the Disabled. In an article in 'Ugeskrift for Læger' dated 18 March 1920, Scheuermann gave the first description based on roentgen examinations of the wedge-shaped deformity and the irregularity of the vertebral body and the epiphyseal plates, the characteristic findings in juvenile dorsal kyphosis. This enabled him to distinguish the syndrome from other forms of humpback and to show that the condition was not due to a weakness of the musculature of the back, as was the common belief. Scheuermann considered it to be a lesion in the growth line between the vertebral body and the epiphyseal plates, and he drew a parallel between the lesion and Calvé-Perthe's disease of the hip.

Overloading might play a part as a contributory cause in many cases. After it had been demonstrated that prolapse of the nucleus pulposus is often present in juvenile kyphosis (Schmorl), Scheuermann formed the opinion (1934) that the wedge shape was a result of the cartilaginous plate of the disk being pressed anteriorly into the vertebral spongiosa.

The University of Copenhagen rejected his dissertation on juvenile dorsal kyphosis as a thesis for his doctorate degree on two occasions; to a great extent the reason lay in the form in which it had been submitted. It is well known that Scheurmann's original observations have subsequently been verified by numerous investigations. It would also be true to say that these have added little of importance to his description nor have they clarified the actual cause of the disease. Scheuermann's name is associated with juvenile dorsal kyphosis in the medical literature of the world.

Scheuermann published a number of valuable articles on neuroroentgenologic subjects from the Military Hospital: the diagnosis of cerebral tumours, sella changes in pituitary adenomata, measurements in roentgen films of the optic canal and of the interpeduncular distances in spinal tumours. While at Sundby Hospital the study of the temporal bone engaged Scheuermann's particular attention. As his assistant I derived much advantage from his insight and knowledge in this field and it has been an honour to continue the work, ever mindful of the tradition which he left behind.

It had long been suggested in various quarters that the University of Copenhagen should give Scheuermann the degree of doctor honoris causa for his work of 1920 and this suggestion eventually bore fruit in 1959, very late in Scheuermann's life. The degree was conferred upon him at the University Commemoration in November and although very weak he was able to be present to receive it.

The picture in my mind of Holger Scheuermann embodies features of many kinds, perhaps the most outstanding one being his tireless zeal and unbounded interest in the investigation of the many problems which arose in his work, a quality that persisted until very late in his career.

His life was not wholly devoted to science. Music was his passion and in the early years he played the cello with joy and talent at chamber concerts at his home in Hørsholm or in Copenhagen. He was a kind and considerate chief who was loved by his staff, whom he had the gift of attaching to himself by the bonds of friendship, and held in regard by his colleagues and the patients. All honour to his memory.

Th. Rosendal

FROM THE DEPARTMENT OF NEUROSURGERY (DIRECTOR: PROF. H. OLIVECRONA) AND THE ROENTGEN DEPARTMENT (DIRECTOR: PROF. E. LINDGREN), SERAFIMERLASARETTET AND KAROLINSKA INSTITUTET, AND THE DEPARTMENT OF PHARMACOLOGY (DIRECTOR: PROF. B. UVNÄS), KAROLINSKA INSTITUTET, STOCKHOLM, SWEDEN

CIRCULATORY DISTURBANCES DURING CEREBRAL ANGIOGRAPHY

An experimental evaluation of certain contrast media

by

ERIK KÅGSTRÖM, PERCY LINDGREN and GUNNAR TÖRNELL

Cerebral angiography, as is well known, is a method of examination not altogether devoid of complications. Unfortunately no contrast medium exists which is pharmacologically quite inert; indeed, this factor is probably responsible for a large proportion of the side effects that have been observed. As regards the action of contrast media, considerable attention has been devoted to the cerebral vessels. Due to the lack of simple and general means for recording the cerebral blood flow, vascular reactions to contrast media have been investigated by numerous methods and under widely varying experimental conditions. Hence, it is not surprising to find contradictory reports. Some authors, for instance, consider that iodopyracet produces cerebral vasoconstriction in carotid angiography, others that it causes vasodilatation. This will be dealt with further in the discussion.

Virtually all our knowledge of the cerebral blood flow during carotid angiography derives from experimental investigations in animals. In human sub-

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jects the methods so far employed have chiefly consisted of roentgenologic studies of the circulation time in the brain, for in recent years high-speed film changers have made it possible to obtain roentgenograms at short intervals and thus to trace the paths followed by the contrast medium during angiography. Since investigations of this type shed no appreciable light on the cerebral blood flow, they will not be treated in this context.

On the other hand, animal experiments with such techniques as studies of the pial vessels through a Forbes' window, thermoelectric method for measuring the dissipation of heat from thermocouples inserted into the brain tissue, as a criterion of the blood flow, direct recording of the flow in the sagittal sinus, etc, can yield direct information on the cerebral circulation, and have been reviewed more extensively in an earlier paper (KÅGSTRÖM, LINDGREN & TÖRNELL 1958).

Studies of the permeability may be satisfactory for elucidating the vascular toxicity of contrast media although not for investigating the cerebral blood flow (for references, see for instance BROMAN & OLSSON 1956). Permeability disturbances are, however, of considerable interest in discussions of the cerebral blood flow as to the danger of edema of the brain, and increased intracranial pressure with secondary circulatory disturbances.

In a series of papers MARGOLIS and co-workers (MARGOLIS et coll. 1958, TINDALL et coll. 1958) compared the toxic effects of several contrast media used in cerebral angiography. They studied injuries of the nervous system (canine spinal cord) using a histologic technique, and concluded that sodium acetrizoate was the most toxic agent, sodium diatrizoate was fairly atoxic, other agents being intermediate. In a recent paper (MARGOLIS et coll. 1959) they demonstrated the vasodilator effect of sodium acetrizoate on vessels in the spinal cord and discussed the vasotoxic effect of the contrast medium correlated to its ability to cause neurologic complications.

We recently reported a comparative investigation of the cerebral blood flow in cats during carotid angiography with the two contrast media, sodium acetrizoate and sodium diatrizoate, using a method described by INGVAR & SÖDERBERG (1956 and 1957) for recording the venous flow in the sagittal sinus. We observed a marked increase of flow after the injection of sodium acetrizoate but no change following sodium diatrizoate. However, the results were spread over a wide range and, although the blood flow often rose three- or fourfold after the injection into the common carotid artery of 0.2 to 0.4 ml sodium acetrizoate 50 %, not even higher doses had any appreciable effect in some experiments. We feel that the causes were chiefly methodologic, as for example a varying distribution of the contrast medium in the region drained via the sagittal sinus.

The present investigation was undertaken in order to ascertain whether sodium acetrizoate does in fact have a constant vasodilator action on cerebral vessels. We performed the experiments in dogs instead of cats, for the dog

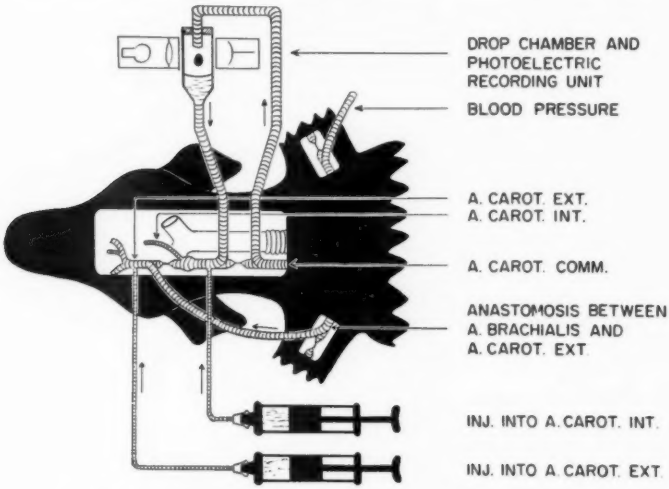

Fig. 1. Schematic representation of the neck preparation of the animals.

has a well developed internal carotid circulation, whereas the cat usually lacks a functioning internal carotid artery. Selective internal carotid angiography is thus possible in dogs.

Since the majority of earlier studies on the cerebral blood flow during carotid angiography had been concerned with iodopyracet, we tested that agent for purposes of comparison, in addition to sodium diatrizoate and sodium diprotrizoate which chemically are closely related to sodium acetrizoate.

Methods

The experiments were performed on seven mongrel dogs weighing from 3.5 to 7.6 kilograms. Following anesthetization with Dial (50 to 70 mg/kg), the ventral part of the neck was dissected with the insertion of a branched tracheal cannula and exposure of both common carotid arteries as well as their branches to a point 2 to 3 cm distal to the carotid sinus. The blood flow in the internal carotid artery was measured by a direct method (photoelectric drop recording) which had previously been used mainly for recording venous blood flow (LINDGREN & UVNÄS 1954). Since this method has certain drawbacks, when applied on the arterial side, an improved modification described by LINDGREN (1958) was employed in the later experiments. After division of the common carotid artery, the drop chamber was connected to its proximal and distal stumps, as shown by the schematic representation in Fig. 1. Peripheral to the drop chamber all branches, except the internal carotid artery, were ligated. To maintain physiologic conditions, as far as possible, in the intra- as well as the extracerebral circulation, the axillary and external carotid arteries were, however, brought into communication via a polythene tube. The injections for the internal carotid artery were made through a slender polythene

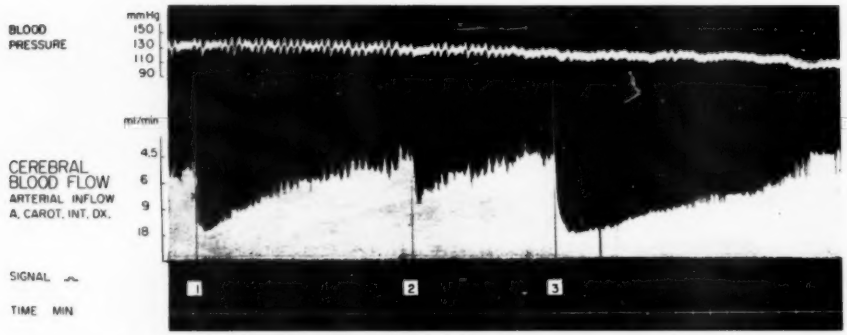

Fig. 2. Dog VI 7.4 kg. Dial 60 mg/kg. Increase of cerebral blood flow during carotid angiography with different contrast media:

1. Iodopyracet (Umbradil) 50 % — 0.2 ml
2. Sodium diatrizoate (Hypaque) 50 % — 0.2 ml
3. Sodium acetrizoate (Triurol) 50 % — 0.2 ml

catheter inserted retrogradely into the superior thyroid artery distal to the drop chamber. A similar injection catheter was placed in a ligated minor branch of the external carotid artery.

If this method, i. e. measurement of the blood flow in the internal carotid, is to provide an indication of the cerebral circulation, it must be ascertained whether the first-named flow is distributed to cerebral regions alone or whether part of it passes to extracerebral areas. For this purpose the experiments were concluded with ordinary angiography with either single or serial roentgenograms.

In some experiments we measured concurrently the blood flow in the sagittal sinus, using the method of INGVAR & SÖDERBERG (1956 and 1957), which we had already employed in an investigation in cats (KÅGSTRÖM et coll. 1958). Each of these methods necessitates heparinization, for which purpose we administered 25 mg/kg Heparin 5 % intravenously. The blood pressure was recorded by a conventional mercury manometer connected to the brachial artery.

The following contrast media were used: Umbradil 50 % (Astra), iodopyracet (also marketed under the proprietary names of Diodone, Diodrast, Perabrodil, etc), Triurol 50 % (Leo), sodium acetrizoate (also marketed under the proprietary names of Acétiodone, Diaginol, Rheopak, Urokon, etc), Hypaque 50 % (Winthrop), sodium diatrizoate, and Miokon 50 % (Mallinckrodt), sodium diprotrizoate.

Results

Effects on the cerebral blood flow. Although the bodyweights ranged from 3.5 to 7.6 kg, the resting blood flow in the internal carotid artery was relatively uniform: 4 to 6.5 ml/min, and usually 5 ml/min; in the lightest and heaviest of the dogs it amounted to 4 and 5 ml/min respectively. The likeliest explanation of this uniformity is that the brain volume of small dogs varies relatively less than the bodyweight — an observation which has also been made in another

Table

Increase of cerebral blood flow (in per cent of the resting level) after intracarotid injection of different contrast media

		Sodium Diatrizoate (Hypaque)	Sodium Diprotrizoate (Miokon)	Iodopyracet (Umbradil)	Sodium Acetrizoate (Triurol)
Dog I.	7.6 kg 0.05 ml	0	25	20	210; 140
	Dial 50 mg/kg 0.1 ml	15	50	90	240; 240
	0.2 ml	40	45	95	240
Dog II.	6.7 kg 0.1 ml	25; 0		105	200
	Dial 55 mg/kg 0.2 ml	55	65		230
Dog III.	5.1 kg 0.1 ml	65		150; 200	330
	Dial 55 mg/kg 0.2 ml	100			
Dog IV.	6.3 kg 0.05 ml				255
	Dial 70 mg/kg 0.1 ml	0	0	45	
	0.2 ml	15	25	45	
Dog V.	3.5 kg 0.1 ml	90	90	220	370
	Dial 70 mg/kg				
Dog VI.	7.4 kg 0.1 ml			165	
	Dial 60 mg/kg 0.2 ml	80		235	300
Dog VII.	4.8 kg 0.2 ml	60			245
	Dial 55 mg/kg				

investigation (Eliasson, Lindgren & Uvnäs 1952). It seemed to us therefore more correct to indicate total dosages of contrast media, the same for different animals, than to dose in milliliters per kilogram of bodyweight. The amounts administered were comparatively small: 0.05, 0.1 or 0.2 ml, corresponding to approximately 0.5 to 3.0 ml in human subjects.

We tried to limit the number of injections per animal, since the cerebral blood flow may change in the course of a long experiment, due not least to the toxic action of the contrast media on the blood vessels. Broman, Forssman & Olsson (1950) called attention to the increasing vascular permeability with repeated doses and Kågström & Lindgren (1960) showed that sodium acetrizoate causes a rise of intracranial pressure which, with repeated doses, may be persistent. Having regard to these findings, the agents with the least vascular activity were usually administered first.

A typical experiment is illustrated in Fig. 2. Three contrast media were investigated: iodopyracet, sodium diatrizoate, and sodium acetrizoate. Each of these raised the cerebral blood flow, the rise beginning only a few seconds after the injection and reaching its maximum after one-half to one minute,

following which the blood flow gradually returned to its original level. (The brief initial 'decrease' of blood flow was not a real one but a methodologic artifact, for since the dose of contrast medium was injected peripheral to the drop chamber, it failed to be recorded. During the course of the injection the intervals between drops were thus prolonged commensurately with the injected volume.) The contrast media differed greatly in their vasodilator effects. It will be seen from the figure that after injection the maximum blood flow was 15 ml/min for iodopyracet, 8.5 ml/min for sodium diatrizoate, and 18 ml/min for sodium acetrizoate, the resting flow having been about 5 ml/min. The time elapsing until the return of the flow to normal seemed to bear some relation to these peaks. The effect of sodium acetrizoate, for example, persisted for no less than 15 minutes.

The results of all experiments are set forth in the Table on p. 7. Sodium diatrizoate and sodium diprotrizoate had the weakest vascular effects; iodopyracet occupied an intermediate position, and sodium acetrizoate consistently produced a marked vascular activity. In view of the previous investigation (KÅGSTRÖM et coll. 1958), which had been concerned solely with sodium acetrizoate and sodium diatrizoate, most of the injections were given with those agents and far fewer with iodopyracet and sodium diprotrizoate. The reason for using sodium acetrizoate only in small doses, in some experiments, was that because of its high vascular activity we desired to avoid an irreversible effect on the cerebral circulation.

In some experiments the blood flow was also recorded in the sagittal sinus. The increased rate of flow in the sinus which followed intracarotid injections was always much smaller than the concurrent one in the internal carotid artery; occasionally the flow in the sagittal sinus was quite unchanged despite ordinary reactions on the arterial side. An experiment with both arterial and venous recording is illustrated in Fig. 3. It will be seen that a 370 per cent rise (from 4.5 to 21 ml/min) of the flow in the internal carotid artery following the injection of 0.1 ml sodium acetrizoate coincided with an increase of only 60 per cent (from 4.5 to 7 ml/min) in the sagittal sinus flow. The causes of this discrepancy are discussed below. Subsequent angiography in the same dog showed contrast filling only of intracerebral vessels.

Effects on the systemic circulation. Although the chief aim of this investigation was to study the cerebral blood flow during carotid angiography, the blood pressure responses were also recorded, partly because major fluctuations in the systemic blood pressure may affect the cerebral blood flow and partly in view of the responses previously noted by GREITZ (1956), LINDGREN & TÖRNELL (1958), and LINDGREN (1959), during similar procedures.

Only in angiography with sodium acetrizoate did appreciable falls of blood pressure occur. They were usually of short duration and amounted to 15 to 25 mm Hg, though occasionally we found no change whatsoever.

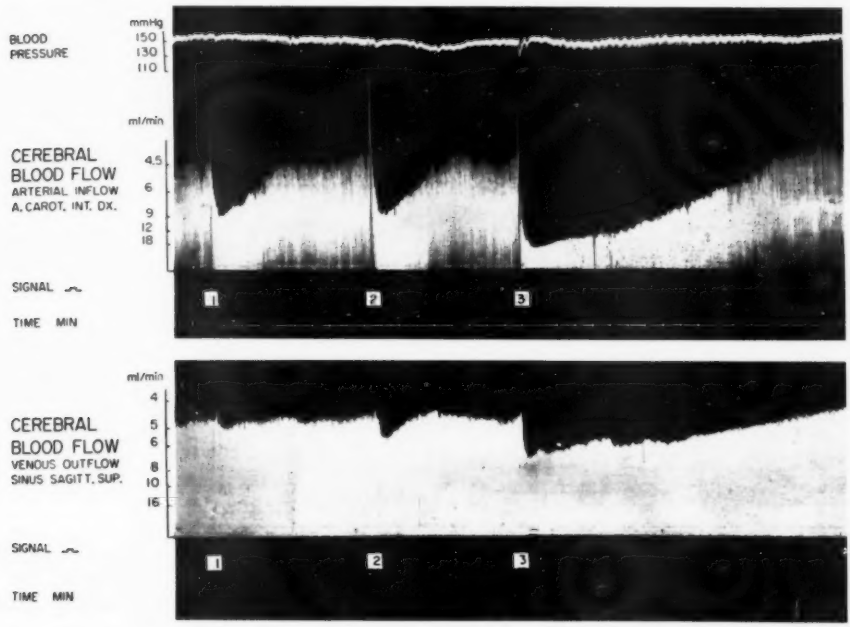

Fig. 3. Dog V 3.5 kg. Dial 70 mg/kg. Cerebral blood flow during carotid angiography. Comparison of the flow changes in the internal carotid artery with those in the sagittal sinus.

1. Sodium diatrizoate (Hypaque) 50 % — 0.1 ml
2. Sodium diprotrizoate (Miokon) 50 % — 0.1 ml
3. Sodium acetrizoate (Triurol) 50 % — 0.1 ml

With the smaller doses (0.05 to 0.1 ml) of iodopyracet, sodium diatrizoate, and sodium diprotrizoate, the blood pressure was not affected; with the higher dose of 0.2 ml a slight fall (5 to 15 mm Hg) was sometimes observed.

We did not check the cardiac activity systematically for bradycardia or electrocardiographic changes, though in one or two instances moderate bradycardia was noted following the injection of sodium acetrizoate — a reaction similar to that which we have earlier reported in cats (LINDGREN & TÖRNELL 1958).

Distribution of blood from the internal carotid artery. Since we considered it important for the evaluation of the results to know the distribution of the substances injected into the internal carotid artery, the experiments were concluded with ordinary angiography. We usually injected a greater amount of

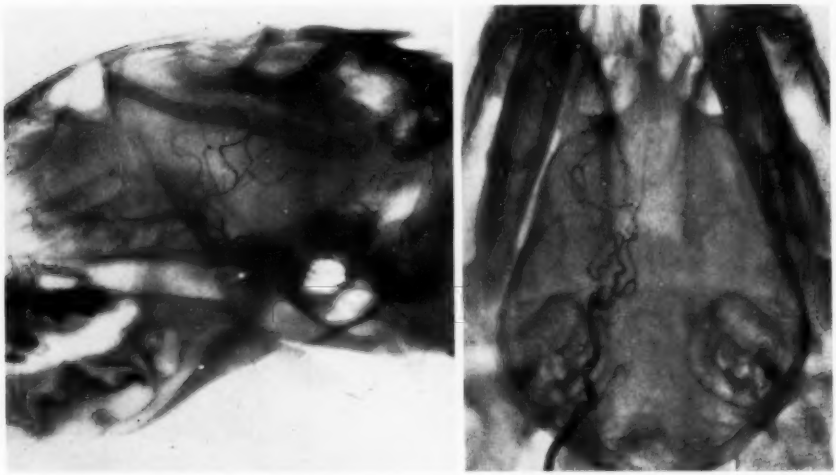

Fig. 4. Angiography of the internal carotid artery in dog showing the distribution of blood from this artery.

contrast medium than in the tests, and also used a higher injection rate and pressure. Hence the observed region of distribution of the internal carotid branches could not possibly be smaller than that into which the test contrast media had passed, and the latter agents were unlikely to have entered any vascular area that was not contrast filled in the angiograms, excepting vessels with such attenuated filling as to be indiscernible. The same applies to our external carotid angiographies. As is evident from Fig. 4, we managed to obtain satisfactory contrast filling of the internal carotid artery and its intracerebral branches. Fig. 5 depicts a similar angiography of the external carotid artery.

Seven dogs were subjected to internal carotid angiography. Major blood vessels that were usually filled with contrast medium included the anterior cerebral and pericallosal arteries, the middle cerebral and, in two dogs, the posterior cerebral artery. Retrograde filling of the basilar artery was twice observed. In five cases the internal carotid flow had a purely intracerebral distribution; a communication to branches of the external carotid (internal maxillary) artery was found in two cases.

In four dogs, only arteries of the ipsilateral hemisphere were filled and in three dogs arteries on the contralateral side as well. One dog showed a good communication with total filling of the circle of Willis including the contralateral anterior and middle cerebral arteries. It is improbable that communication

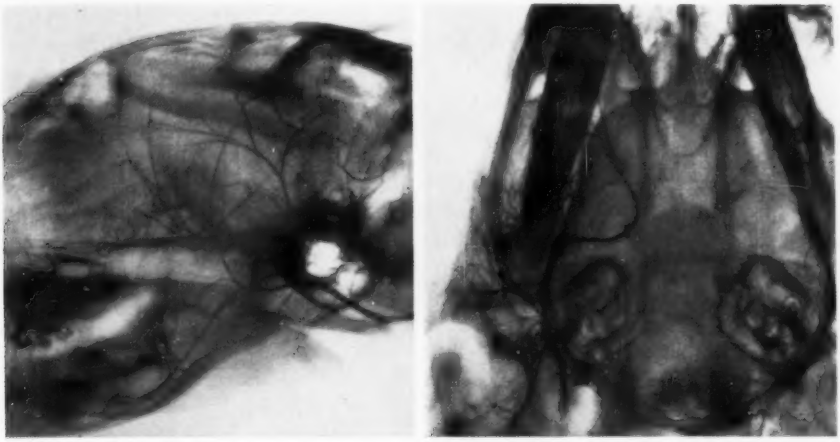

Fig. 5. Angiography of the external carotid artery of the same dog as in fig. 4.

to the contralateral part of the circle of Willis plays any role under physiologic conditions. An explanation might have been a low blood pressure when the final angiography was performed. If the injection had caused an elevation of the blood pressure in the internal carotid artery of that side, it is possible that a difference in pressure might have facilitated a contralateral contrast filling (vide SALTZMAN 1959). In two dogs, the anterior cerebral artery was the only contralateral vessel that was filled.

In the external carotid angiographies we found that only extracerebral vessels were filled, except in one dog in which filling also of the intracranial portion of the internal carotid and of the middle cerebral artery was obtained. Communicating branches of the external carotid artery are not likely, therefore, to play any major part in the normal blood supply of the canine brain.

Summarizing, the external and internal carotid systems in the dogs are fairly well separated. Thus the internal carotid blood has almost solely an intracerebral distribution, which means that the method presented does in fact record the magnitude of the cerebral blood flow.

Discussion

In our previous investigation (KÅGSTRÖM, LINDGREN & TÖRNELL 1958) of the cerebral blood flow during carotid angiography with sodium acetrizoate in cats, the results, as a rule consisting in an increase of the venous outflow

from the sagittal sinus, were dispersed over a wide range. Indeed we often found no increase of flow at all, despite injection of fairly high doses of the medium (0.4 ml). We attributed this state of affairs to the experimental conditions and did not believe that the contrast medium itself had such varying vascular effects. These experiments in cats had several shortcomings. In the first place the injections were made into one of the common carotid arteries so that the contrast medium passed to both extracerebral and intracerebral areas, the intracerebral dose being impossible to determine; secondly, the blood flow was recorded in the sagittal sinus which drains parts of both hemispheres, the areas varying in extent in different subjects.

The present method has fewer drawbacks. The dog, unlike the cat, possesses a functioning internal carotid artery and if selective distribution to intracerebral structures alone is desired, the injections can be made directly into that vessel. In recording on the arterial side, the measured blood flow reflects the vascular resistance throughout the region to which the contrast medium is distributed. In venous recording it is often difficult by intra-arterial injection to distribute the solution to the whole of the venous drainage area. This circumstance must be taken into account in the case of all vascular areas, but especially so in studies of the cerebral blood flow.

The significance of the above considerations is exemplified by the results of the experiment in which the two recording methods were employed concurrently (Fig. 3). The greater sensitivity of arterial recording is clear. With minor changes of blood flow in the internal carotid artery (on injection of sodium diatrizoate and sodium diprotrizoate) the sagittal sinus flow was scarcely altered at all; not until the arterial flow rose substantially (on injection of sodium acetrizoate) did the venous flow increase, though to a lesser degree than the former.

In several papers on the cerebral blood flow and vascular responses to various drugs, it has been pointed out that the reactions are far weaker than those in other vascular areas (for references, see SCHMIDT 1950). Without discussing in detail the pharmacology of the cerebral circulation, it is worth noting that vasodilatation associated with such a marked increase in flow as that which follows the injection of sodium acetrizoate has not been described earlier, with the possible exception of the well known effect in the case of carbon dioxide.

The results of the present investigation are unequivocal. There should no longer be any doubt that carotid angiography with sodium acetrizoate in the dog and cat is attended by considerable increase in the cerebral blood flow, whereas the contrast media sodium diatrizoate and sodium diprotrizoate are less active in this respect.

Iodopyracet, which occupies an intermediate position with regard to its vascular effects, is interesting insofar as it has been mainly employed in most of the previous studies on the influence of contrast media upon the cerebral

blood flow. Contradictory findings are common; some authors consider that carotid angiography with iodopyracet gives rise to vasospasm or vasoconstriction, others that vasodilatation occurs. The former group includes FOLTZ, THOMAS & WARD (1952), who observed (Forbes' window) the following reaction of the pial vessels in monkeys and cats: 'Severe vasospasm lasting a few seconds; cortical pallor 60—90 seconds, followed by a cortical blush during 1—2 minutes'. The amounts of contrast medium which they injected were, however, very large — 2.5 ml Diodrast 35 or 70 % in cats. BROMAN & OLSSON (1948), using a similar technique, had earlier observed a retardation of the flow in the pial vessels following the intracarotid injection of iodopyracet, but had attributed the reaction largely to the high viscosity of the injected solution. INGVAR & SÖDERBERG (1957) found cerebral vasoconstriction after the intracarotid injection of iodopyracet (cats, 0.5 ml Umbradil 35 %, recording of the flow in sagittal sinus). In a later paper, however, SÖDERBERG & WECKMAN (1958) partially re-interpreted these results and thought that the observed reduction of the sagittal sinus flow might have been due in part to extracerebral vasodilatation caused by the contrast medium, with a secondary fall in the intracranial arterial pressure and a consequently decreased blood flow.

The other group of authors found, as we have done, that iodopyracet produces cerebral vasodilatation. Amongst these investigators, who used varying methods, were BLOOR, WRENN & MARGOLIS (1954), BROWNE & STERN (1954), and SCHMIDT (1955).

The diversity of opinion may well be due to the varying experimental conditions. It illustrates the difficulty of finding a really suitable experimental method for studying the cerebral circulation. The technique that we employ has, we feel, several advantages in that the determination of the blood flow is direct, quantitative, and continuous, and the subsequent angiography provides good information regarding the arteries and regions to which the measured blood has been distributed — largely to the intracerebral structures alone.

It is difficult to evaluate the clinical importance of the observed major differences between the vascular actions of the various contrast media. Several comparative investigations have been published regarding the incidence of side effects and complications in patients (e. g. ODÉN 1955, BROADBRIDGE 1956, WHITELEATHER & DE SAUSURE 1956). It is an open question whether the clinically demonstrable side effects can be correlated with the vascular reactions. Although an increased cerebral blood flow as such, following angiography with e. g. sodium acetrizoate, is unlikely to heighten the danger of complications, interest nevertheless attaches to BROADBRIDGE's (1956) observation that sodium diatrizoate caused far less discomfort than did sodium acetrizoate or iodopyracet. According to our results, sodium diatrizoate has the least vascular activity of the three. Thus it seems plausible that there is a correlation between the vascular activity of the contrast medium and the clinical complications reported.

Conclusions

The following results were obtained:

1. The internal carotid blood had largely an intracerebral distribution in the ipsilateral hemisphere. Communications with extracerebral vessels were usually of no major importance.

2. Sodium acetrizoate (Triurol) in doses of 0.1 to 0.2 ml had consistently a considerable vascular effect with an increase of the blood flow by 200 to 400 per cent. The duration of this effect was approximately 12 minutes.

3. Iodopyracet (Umbradil) in the same doses had a weaker effect with an increase in most cases by 100 to 250 per cent, the duration being about 6 minutes.

4. Sodium diatrizoate (Hypaque), usually had only a slight effect on the blood flow, the increase never exceeding 100 per cent. The duration was short, about 2 minutes.

5. Sodium diprotrizoate (Miokon), had essentially the same effects as sodium diatrizoate.

6. In simultaneous recording of the internal carotid and the sagittal sinus blood flows, the former method was the more satisfactory for our purpose.

7. It is concluded that the discrepancy among earlier results (vasoconstriction or vasodilatation after cerebral angiography) is attributable to varying methods and experimental conditions.

8. With the small doses used, the effects of carotid angiography on the systemic blood pressure were relatively small. Only sodium acetrizoate caused a transient fall of 15 to 25 mm Hg.

Acknowledgement

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SUMMARY

The cerebral blood flow was studied in dogs during internal carotid angiography, with four different contrast media, by measuring the blood flow in the internal carotid artery by a special method. Of the contrast media investigated sodium acetrizoate was the most potent vasodilator, sodium diatrizoate and sodium diprotrizoate the weakest, with iodopyracet occupying an intermediate position. Attention is drawn to a certain relationship between the vascular actions of different contrast media and clinically observed side effects.

ZUSAMMENFASSUNG

Die cerebrale Blutzirkulation wurde an Hunden mittels Angiographie der A. carotis int. mit 4 verschiedenen Kontrastmitteln studiert, wobei der Blutstrom in der A. carotis int. mit einer Spezialmethode gemessen wurde. Von den angewandten Kontrastmitteln erwies sich

Natriumacetrizoat als der wirksamste Vasodilatator, Natriumdiatrizoat und Natriumdiprotrizoat als die schwächsten, während Jodopyracet eine Mittelstellung einnahm. Besondere Aufmerksamkeit wurde einem gewissen Zusammenhang der vaskulären Wirkung der Kontrastmittel und ihren klinisch beobachteten Nebenwirkungen gewidmet.

RÉSUMÉ

Le débit cérébral au cours de l'angiographie carotidienne interne avec quatre moyens de contraste différents a été étudié sur des chiens en mesurant le débit de l'artère carotide interne par une méthode spéciale. Parmi les moyens de contraste étudiés, l'acétrizoate de sodium est le plus puissant vasodilatateur, le diatrizoate de sodium et le diprotrizoate de sodium sont les plus faibles, l'iodopyracet occupant une position intermédiaire. Les auteurs attirent l'attention sur une certaine relation entre les effets vasculaires des différents moyens de contraste et les effets secondaires observés cliniquement.

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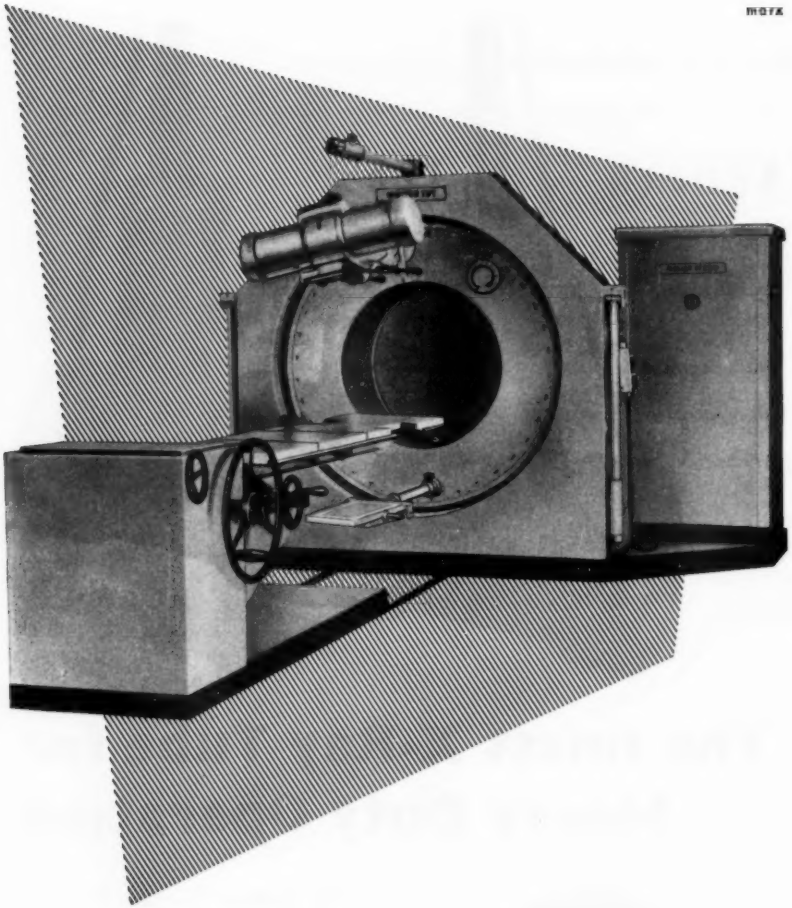

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FROM THE ROENTGENDIAGNOSTIC DEPARTMENT (DIRECTOR: PROF. SÖLVE WELIN),
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EMPTYING EFFECT ON THE GALLBLADDER OF TWEEN 80

by

LARS ANDRÉN and GEORG THEANDER

Tween is the name given to certain non-ionic wetting agents consisting of polyethylene oxide linked with, e. g. monolaurate (Tween 20), monopalmitate (Tween 40), monostearate (Tween 60), or monooleate (Tween 80) of sorbitane. Owing to their low toxicity these agents are widely used as solvents in modern pharmacy (ULLMAN 1957). They were first used in roentgenology with the introduction of Bilijodon capsules (Leo) for oral cholegraphy (GUNNARSON 1959). These capsules contain 0.45 g of the sodium salt of iopanoic acid dissolved in a mixture of 0.25 g Tween 80, 0.24 g polyethylene glycol (polyethylene oxide, Carbowax 400), and 0.23 g dipropylene glycol. After clinical trials a single dose of 1 capsule per 10 kg bodyweight is now recommended by the manufacturer for cholegraphy.

Tween 80 was incorporated in Bilijodon capsules to accelerate the absorption of the contrast medium. It was not supposed to have any significant effect on the digestive system. Tween 60, given clinically in daily doses of 6 g over 28 days, is said not to interfere significantly with the secretory function or motility of the stomach, the occurrence of gas in the bowel, or the emptying of the gallbladder (STEIGMAN et coll. 1953). In our experience, however, Tween 80 has a remarkable influence on the size of the gallbladder.

Material and Results

Bilijodon capsules were used in our department, inter alia, for completion of routine cholecystographies with Bilijodon-Natrium tablets (i. e. the undissolved sodium salt of iopanoic acid). Thus, certain patients, in whom

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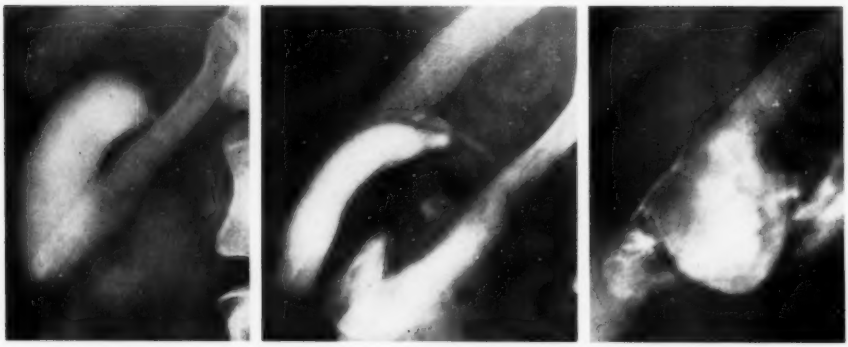

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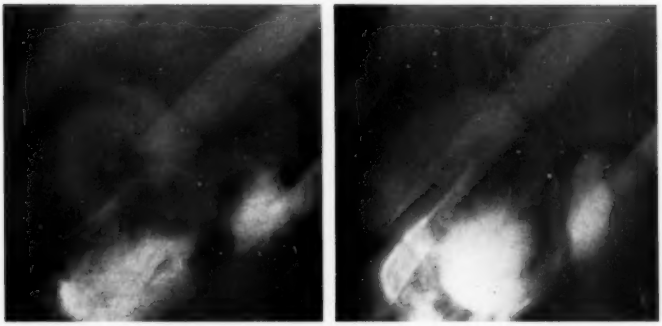
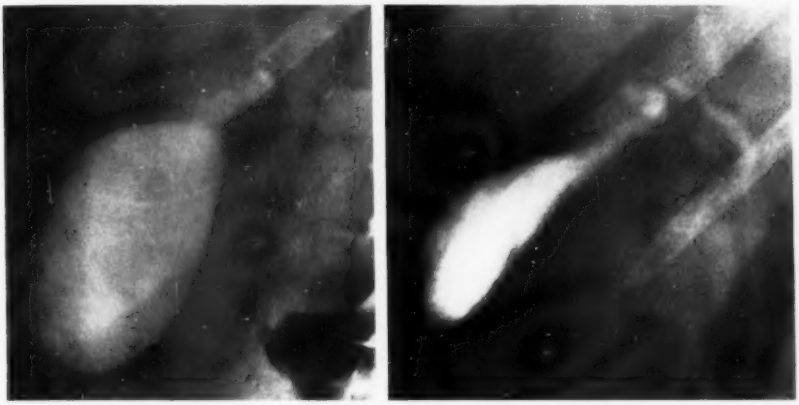


d e

Fig. 1. Cholecystography: a) before, b) 45 min, and c) 2 hours after intake of Bilijodon capsules. Filling of bile ducts and almost complete emptying of gallbladder. Residual contrast medium in the stomach. d) 15, e) 30 min after injection of oxicone-papaverine. Re-filling of gallbladder.

cholecystography alone failed to demonstrate the bile ducts, immediately received Bilijodon capsules (1.5 capsules per 10 kg, i. e. the dose initially recommended). As expected, the bile ducts then became demonstrable, as a rule within ninety minutes. In several cases the gallbladder changed in size after ingestion of the capsules. Thus, in a series of 18 patients the gallbladder was seen to decrease in 4, to increase in 2, and to decrease after an initial increase in 3 cases. In one case the gallbladder emptied almost completely



a b

Fig. 2. Cholecystography: a) before, and b) 90 min after intake of 9 g Tween 80. Filling of bile ducts and incomplete emptying of gallbladder.

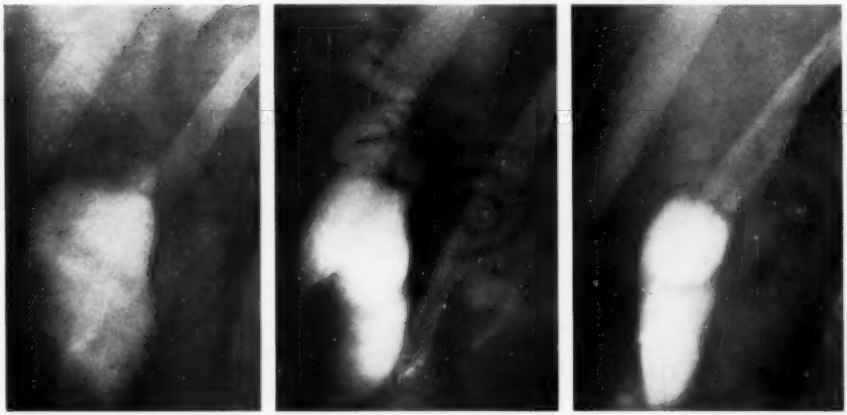
and then re-filled with contrast medium (Fig. 1). The emptying effect of the Tween could be counteracted by oxicone-papaverine.

The above observations prompted further experiments with each of the three solvents incorporated in the Bilijodon capsules. Gelatine capsules, similar to those used for the original preparation, but filled with only one of the solvents, were supplied by AB Leo. They were given in single doses of 1 capsule per 10 kg bodyweight to patients examined with Bilijodon-Natrium tablets or other cholecystographic contrast media. Only a few experiments were carried out with polyethylene glycol and dipropylene glycol. The former solvent had no appreciable effect on the size of the gallbladder; the latter a slight but inconstant effect. Tween 80 (0.15 g/kg), on the other hand, invariably caused a striking contraction of the gallbladder; in 8 of 9 patients examined the bile ducts were demonstrable (Figs 2 and 3).

A further series of 15 patients received Tween 80 in smaller doses (6 g in 5 and 4.5 g in 10 cases). Even then the gallbladder contracted regularly though less markedly. The bile ducts were demonstrable in 3 cases only.

The emptying effect of Tween 80 was usually first apparent at 10 to 30 min, and most obviously at 30 min to 2 hours, after the intake of the capsules. In 5 patients examined at more than 2 hours the gallbladder was observed to be re-filled with contrast medium.

No serious side-effects were observed.



a b c

Fig. 3. Cholecystography: a) before, b) 30 min, and c) 90 min after intake of 9 g Tween 80. Filling of bile ducts and incomplete emptying of gallbladder.

Discussion

In human subjects up to about 95 % of orally administered Tween 80 is passed unchanged in the stools, whereas roughly 5 % is excreted in the urine as polyethylene oxide (CULVER et coll. 1951). The decomposition is thought to occur in the digestive tract under the influence of pancreatic enzymes. Polyethylene oxide given intravenously appears to have no pharmacologic effects in man or animals (SMYTH et coll. 1945, 1947 and 1950, SHAFFER et coll. 1947 and 1950, SHIDEMAN & PROCITA 1951, MEYER & STÜRMER 1952). In the present investigation the patients had fasted after the intake of contrast medium on the evening before the examination. It seems less likely, then, that Tween 80 provoked the observed emptying of the gallbladder by accelerating the absorption of any cholecystokinetic substance. More probably the fatty acid component in the Tween 80 molecule played the important role by liberating cholecystokinin.

Judging from the uniform results of the present experiments, Tween 80 may be used with advantage to study the evacuation capacity of the gallbladder and to demonstrate the bile ducts, provided sufficient contrast medium is present in the gallbladder. When given together with a contrast medium, as in Bilijodon capsules, the substance may possibly improve cholegraphy in two ways, i. e. by accelerating the absorption of contrast medium and by emptying the gallbladder at a suitable moment.

SUMMARY

Evacuation of the gallbladder was observed roentgenographically after the oral administration of Tween 80 in single doses of 4.5 g or more after cholecystography.

ZUSAMMENFASSUNG

Entleerung der Gallenblase wurde röntgenographisch nach oralen Gaben von Tween 80 in Einzeldosen von 4.5 g und mehr im Anschluss an die Cholecystographie beobachtet.

RÉSUMÉ

Les auteurs ont étudié radiographiquement l'évacuation de la vésicule biliaire après administration orale de Tween 80 par doses uniques de 4.5 g ou plus après cholécystographie.

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SKULL CHANGES IN EIGHTEEN CASES OF DYSTROPHIA MYOTONICA

by

GIOVANNI DI CHIRO and JOHN EGERTON CAUGHEY

Dystrophia myotonica (myotonica atrophica) is a heredofamilial disorder which is inherited as an autosomal dominant. When the disease first appears in a family, it presents with cataract. This may be the only detectable evidence of the disease in one or two or maybe three generations. Usually, however, in the second or so-called dystrophic generation, the cataract develops at an earlier age and other features of the fully developed disorder appear, such as myotonia, muscle wasting, gonadal atrophy, frontal baldness, and cardiac abnormalities of conduction and rhythm.

Few authors have referred to the radiographic changes in the skull in these patients. SCHARNKE and FULL (1920) reported in one case large frontal sinuses with a normal pituitary fossa. ROUQUÈS (1931) described the skull roentgenographic findings in four patients with dystrophia myotonica but did not emphasize this as an aspect of the disorder. In his cases there was thickening of the calvaria in three, in two the sella turcica was small, in two the frontal sinuses were large, and in two there was a bridged sella. FAGIN (1946) reported hyperostosis frontalis in one male patient. One of us (CAUGHEY & BROWN 1950) in an endocrine study of nine cases of dystrophia myotonica reported on the radiographic skull changes and suggested that these should come to be

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Table

Patient	Age and Sex	Approximate duration of illness in years	Gonadal changes if present	Skull changes		
				General shape	Vault	Paranasal sinuses
1. D. J....	35 ♀	9		0	Thickened calvaria, hyperostosis frontalis interna	Large sphenoidal
2. C. H. ..	35 ♂	13	Tubular atrophy	0	Thickened calvaria in frontal region	Frontal moderately large
3. D. H. ..	44 ♂	5		0	Thickened calvaria in frontal region	Frontal moderately large
4. C. F. ..	18 ♂	10		0	Thickened calvaria	Large sphenoidal
5. E. W. ..	36 ♂	16	Small testicles, tubular atrophy	Acromegaloid	Thickened calvaria	Frontal very large
6. F. K. ..	37 ♀	25	FSH > 172	0	Thickened calvaria	Frontal moderately large
7. P. K. ..	11 ♂	1		0	0	0
8. T. L. ..	29 ♂	1		Acromegaloid	Thickened calvaria	Large frontal
9. J. W. ..	44 ♀	30	Hysterectomy and oophorectomy at 38	0	Thickened calvaria	Frontal absent
10. V. W...	47 ♀	20		0	Hyperostosis frontalis interna	0
11. C. W...	41 ♂	17	Small testicles (No biospy)	Acromegaloid	Thickened calvaria	Large frontal
12. M. T...	33 ♀	15		0	Thickened calvaria	0
13. R. V. ..	22 ♂	4		0	0	0
14. L. W. ..	39 ♂	3	Small testicles, tubular atrophy	0	Thickened calvaria	0
15. F. W ..	49 ♀	4		0	Thickened calvaria, hyperostosis frontalis interna	Small frontal
16. I. B....	35 ♀			0	Thickened calvaria	0
17. J. W. ..	33 ♀	15	FSH > 96	0	Hyperostosis frontalis interna	Small frontal
18. J. U. ..	48 ♂	2	Tubular atrophy	0	Hyperostosis frontalis interna	Large frontal

'0' indicates within normal limits.

accepted as one of the variable features of the disorder. In subsequent papers CAUGHEY (1952) added further case reports. Among twenty-one cases of fully developed dystrophia myotonica, fifteen showed changes in the skull. Thicken-

Fig. 1. Thickened calvaria throughout. Case 6.

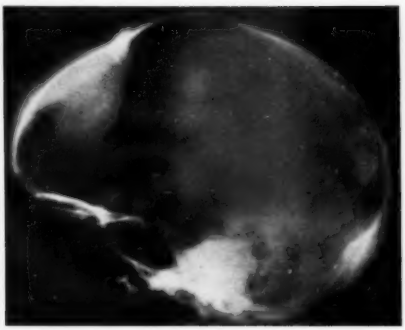

Fig. 2. Thickened calvaria in frontal region. Case 4.

ing of the calvaria and hyperostosis interna were present in eleven cases, large frontal sinuses in eight, a small to very small sella turcica in thirteen, prognathism in three, and calcification of the falx in three. JEQUIER (1950), and DE OLIVEIRA and MOSINGER (1951) also discussed the skull changes in dystrophia myotonica. WALTON and WARRICK (1954) studied seventeen cases and confirmed the high incidence of thickening of the calvaria and the small pituitary fossa. In none of their patients did they find hyperostosis interna and they did not consider enlargement of the frontal sinuses, bridging of the sella, prognathism, or intracranial calcification as being statistically significant.

The object of the present publication is a survey of the skull roentgen films of eighteen cases of dystrophia myotonica which have been investigated at the National Institute of Neurological Diseases and Blindness in the past five years. The records of these patients have been reviewed and the diagnosis of dystrophia myotonica is beyond doubt. Sixteen of the eighteen patients included in the present study had muscle biopsy. Usually the diagnosis of dystrophia myotonica is made on clinical basis: muscle biopsy however may yield strong confirmatory evidence.

Our findings are summarized in the Table on p. 23. Sixteen out of eighteen cases (89 per cent) showed changes of the vault. Such changes which we will indicate for the matter of simplicity with the general term of 'hyperostotic' may be grouped in four different types:

1. Thickened calvaria throughout — nine cases (Fig. 1). This type of change corresponds to what MOORE (1955) indicated as 'hyperostosis calvariae diffusa'.

a b

Fig. 3. Hyperostosis frontalis interna. 'Nodular' appearance of inner surface of frontal bone and unaffected midline 'groove'. a) Case 10, and b) Case 18.

2. Thickened calvaria in the frontal region — two cases (Fig. 2), corresponding to the 'nebula frontalis' of MOORE.

3. Hyperostosis frontalis interna — three cases (Fig. 3). In the frontal region, irregular thick mammillated bulgings of newly formed bone project towards the endocranium, and an unaffected 'groove' along the midline is clearly seen. This type of change corresponds to the 'hyperostosis frontalis interna' of MOORE. However, our criteria for making the diagnosis of hyperostosis frontalis interna are somewhat different. The 'nodular' appearance of the inner surface of the frontal bone as well as the unaffected midline 'groove' are in our opinion important roentgenographic features of this condition.

4. Thickened calvaria throughout and hyperostosis frontalis interna — in two cases (Fig. 4).

These 'hyperostotic' changes of the vault occurred with the same frequency in males and females (eight males and eight females) which is a striking fact when we consider the sex incidence of the large series of cases of hyperostosis cranii reported by HENSCHEN (1949), 99 per cent in women, and by MOORE (1955), 98.2 per cent in women. The age distribution in our series was as follows: second decade, two; third decade, three; fourth decade, seven; and fifth decade, six cases. All patients in the fourth and fifth decades had changes. The two cases without 'hyperostosis' were aged eleven and twenty-two. The more severe cases occurred in women and the longer the duration of the disease,

Fig. 4. Thickened calvaria with some degree of hyperostosis frontalis interna. Case 15.

as gauged by the duration of the patients' symptoms, the more advanced were the 'hyperostotic' changes.

An attempt was made to correlate the hyperostosis cranii with the onset of gonadal atrophy. In four males we had clinical evidence of gonadal atrophy which was confirmed by gonadal biopsy. In one other male the testicles were very small. The assessment of ovarian hypofunctions is more difficult. Two of our female patients, both in their fourth decade, showed a high level of follicle stimulating hormone (greater than 172 mouse units in one and greater than 96 mouse units in the other). In another woman hysterectomy and oophorectomy had been carried out at thirty-eight years of age. In these eight patients who had evidence of gonadal failure, the degree of hyperostotic changes was most marked.

In three of the eighteen cases the shape of the skull was acromegaloid. In seven cases the frontal sinuses were very large, large, or moderately large; in two cases a large sphenoidal sinus was present. No significant elongation of the mandible was found in the present material. The 'small size of the sella' and the intracranial calcifications reported in other publications are not by themselves findings of proven pathological significance.

Concerning possible etiological factors accounting for the 'hyperostotic' changes in patients with dystrophia myotonica, one of us in a previous publication (CAUGHEY 1958) has suggested that hyperostosis cranii, excessive sinus formation, and prognathism are acromegaloid features brought about by

unrestrained activity of growth hormone, released as a result of the gonadal failure. The possible relationship of the hypogonadal function and the degree of skull changes reported in our present series, lends support to this contention. Another possibility is that the skull changes may be on a genetic basis, as a pleiotropic manifestation of a single gene or an expression of involvement of different genes.

Further studies of the problem could include:

1. Radiologic examinations of the skulls of relatives of affected patients.

2. Periodical roentgen examinations of patients with dystrophia myotonica to establish possible progression in the hyperostotic process. Two of the patients of the present series have been roentgen examined on two occasions. The interval between the examinations was two years in one and eighteen months in the second case. After this lapse of time no significant difference was seen in the hyperostotic changes which were present in both of these patients. Muscle lesion had progressed in both cases during the interval between the two admissions.

3. Search for evidence of excessive growth hormone when such measurement becomes available.

SUMMARY

The skull roentgen films of eighteen cases of dystrophia myotonica have been reviewed. Seventeen had 'hyperostotic' changes of the vault, the sex distribution being equal. The longer the duration of the disease the more marked were these changes. In eight cases with proof of hypogonadism the hyperostosis was most advanced. Because of their frequency hyperostotic changes should be considered as one of the variable features of the disease.

ZUSAMMENFASSUNG

Die Schädelaufnahmen von achtzehn Fällen von Dystrophia myotonica wurden eingehend studiert. Siebzehn zeigten hyperostotische Veränderungen der Kalotte, die auf beide Geschlechter gleichmässig verteilt waren. Je länger die Dauer der Krankheit desto ausgeprägter waren die hyperostotischen Veränderungen. In acht Fällen von erwiesenem Hypogonadismus war die 'Hyperostosis' am meisten fortgeschritten. Infolge ihres häufigen Auftretens sollten hyperostotische Veränderungen als variable Erscheinung der Erkrankung angesehen werden.

RÉSUMÉ

Les auteurs ont examiné les radiographies du crâne de dix-huit cas de dystrophie myotonique. Dans dix-sept cas il y avait des modifications 'hyperostotiques' de la voûte, également distribuées dans les deux sexes. Les modifications hyperostotiques étaient d'autant plus marquées que la durée de la maladie avait été plus longue. Dans huit cas présentant un hypogonadisme prouvé, l'hyperostose était très marquée. En raison de leur fréquence, les modifications hyperostotiques devraient être considérées comme un des signes variables de cette affection.

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PAROSTEAL OSTEOGENIC SARCOMA

by

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Parosteal osteogenic sarcoma is a rare variety of osteogenic sarcoma, probably arising in periosteal connective tissue. In 1951, JAFFE and SELIN mentioned the juxtacortical osteogenic sarcoma and stressed its more favourable prognosis as compared to the ordinary osteogenic sarcoma. The same year GESCHICKTER and COPELAND published 16 cases under the designation parosteal osteoma. They considered this lesion to be primarily benign with a tendency to growth and to malignant change. In 1954, DWINNEL, DAHLIN and GHORMLEY reported 15 cases obtained by reviewing 400 cases of osteogenic sarcoma among 2 000 primary bone tumors. They held that this lesion is malignant from its outset, and regarded the term parosteal osteogenic sarcoma as being more appropriate. Minor series of parosteal osteogenic sarcoma have also been recorded in modern textbooks on bone tumors (DAHLIN, JAFFE).

Most authors stress the slow growth, the tendency to recurrence after local excision, and the protracted course of this tumor.

The question of treatment is still a matter of controversy (LICHTENSTEIN). It appears that the parosteal type of growth accounts for about 4 per cent of the osteogenic sarcomas and about 1 per cent of the primary bone tumors

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Fig. 1a—b. Case 1. Parosteal sclerotic tumor of right lower femur 8 years after onset of symptoms.

(DWINNEL et coll.). Our 5 cases have been selected from 85 cases of osteogenic sarcoma among 245 cases of primary malignant bone tumors treated at our hospital during the period 1932 to 1957.

Case reports

Case 1. Female, aged 21, with restricted movement of the right knee for 2.5 years, and a lump at the back of the knee for 3 months. Roentgen examination in 1937 revealed a juxtacortical, sclerotic tumor, partly enveloping the lower end of the right femur. Histology showed some signs of malignancy, and a diagnosis of osteogenic sarcoma of low malignancy was made. Roentgen irradiation was applied; tumor dose approximately 5 000 r. Progression was then first observed in 1943 and supplementary roentgen irradiation of about 2 500 r was given. Further progression was evident one year later, and amputation was performed. The patient died 7.5 years later from a lung tumor, probably metastatic. No autopsy was performed.

The earliest available *roentgenograms*, taken in 1943 (Fig. 1a—b), showed a tumor of the distal

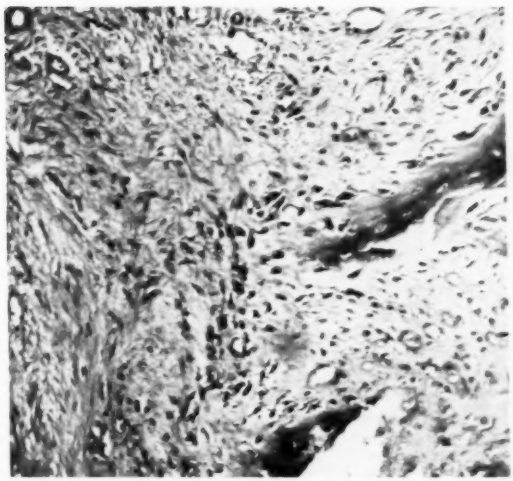


Fig. 1c. Osteogenic sarcoma of low malignancy (× 125).

posteromedial aspect of the right femur, partly encircling the metaphysis. The tumor was densely sclerotic, with an irregular, less dense periphery. No signs of periosteal lipping or true spicules were evident.

Histology in October 1937 (Fig. 1c) showed irregular spicules of bone and osteoid tissue, cartilaginous and myxomatous areas, and a highly vascularized connective tissue containing some large, darkly stained cells. The degree of atypia was moderate. Diagnosis: osteogenic sarcoma of low malignancy.

Case 2. Female, aged 45, with a tumor above the left knee for 3 months. Biopsy in 1950 failed to show any evidence of malignancy, and the tumor was considered to be an osteoma. Excision was performed in February 1952 following progression. There was a recurrence 6 months later and 6 months after this, in 1953, the patient was again admitted. Roentgen examination of the lungs revealed multiple nodular metastases. Irradiation was applied to the femoral tumor, as a palliative measure, but the mass steadily progressed. The patient died from multiple metastases in 1955, 5 years after the onset of symptoms. No autopsy was performed.

Roentgenograms on admission, in 1950, showed a tumor of the lower posterolateral aspect of the left femur, which was dense, broad-based and lobulated. A noncalcified zone was visible between the cortex and part of the tumor. A densely sclerotic cap of tumor tissue posteriorly (Fig. 2, a and b).

Histology. Biopsy from the tumor in April 1950 (Fig. 2c), showed rich bone formation in irregular strands, between which was a highly cellular tissue consisting of spindle cells and polyhedral cells with moderate variations in nuclear size and stainability; only few mitoses were evident. Microscopy of a late cutaneous metastasis revealed an osteogenic sarcoma of a high degree of differentiation (Fig. 2d).

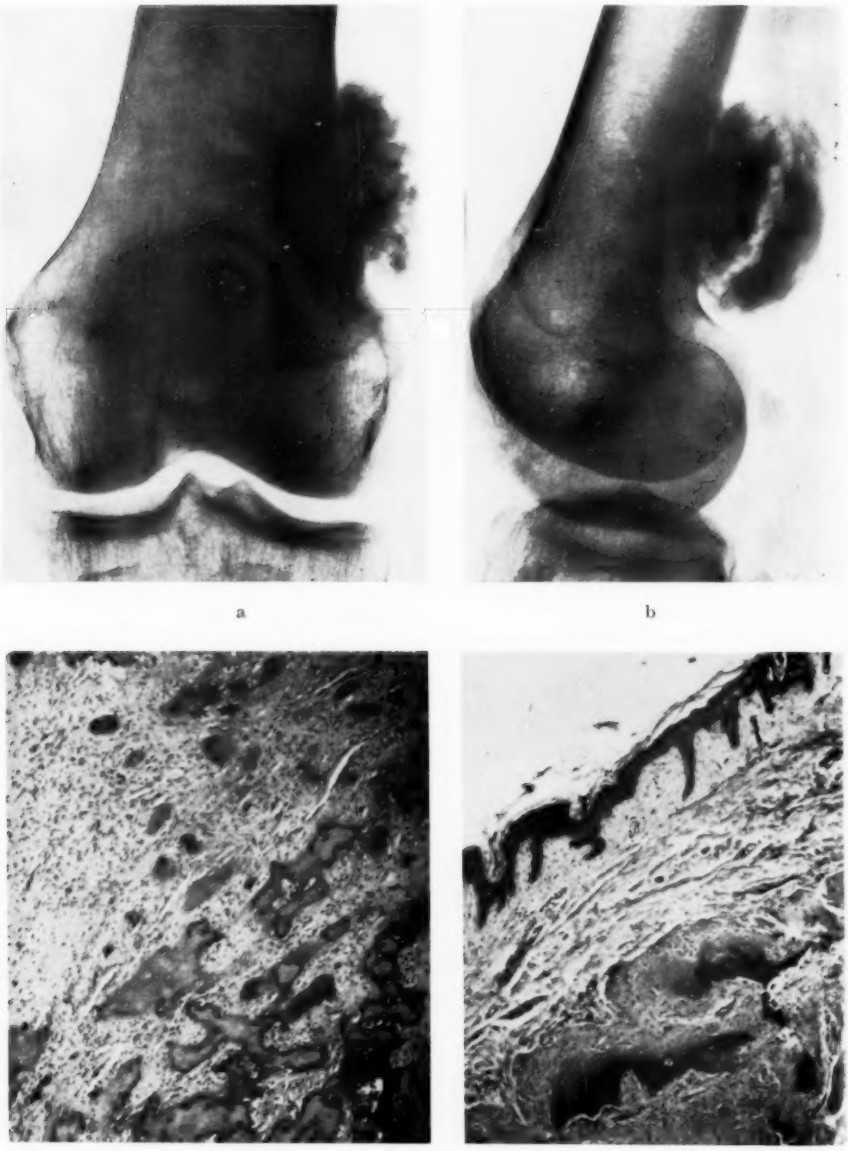


Fig. 2. Case 2. a) and b) Sclerotic tumor of left lower femur. A clear zone is seen between tumor and underlying cortex. c) Irregular osseous trabeculae separated by proliferating connective tissue with moderate atypia. × 50. d) Cutaneous metastasis from highly differentiated osteogenic sarcoma. × 50

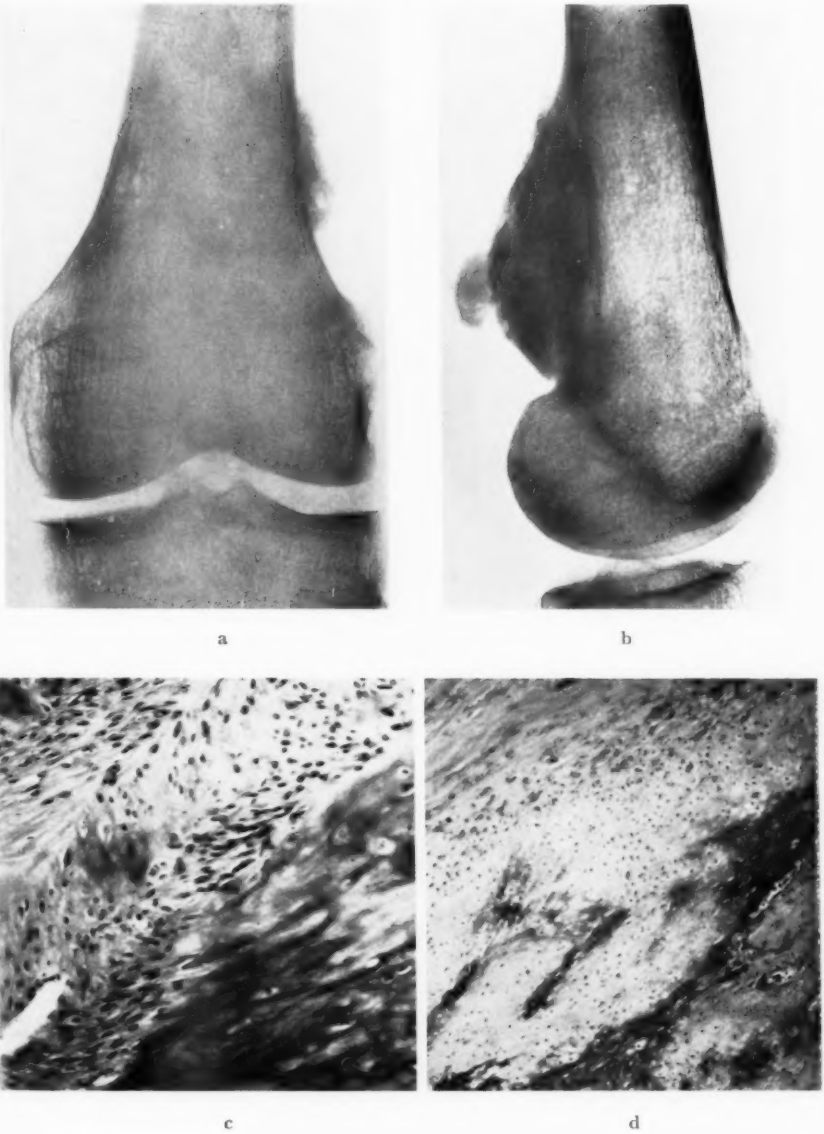


Fig. 3. Case 3. a) and b) Parosteal sclerotic tumor of left lower femur discovered immediately after an injury. c) Atypical cartilage and osteoid and connective tissue. × 125. d) Amputation specimen. Irradiated osteogenic sarcoma. × 50.

a b

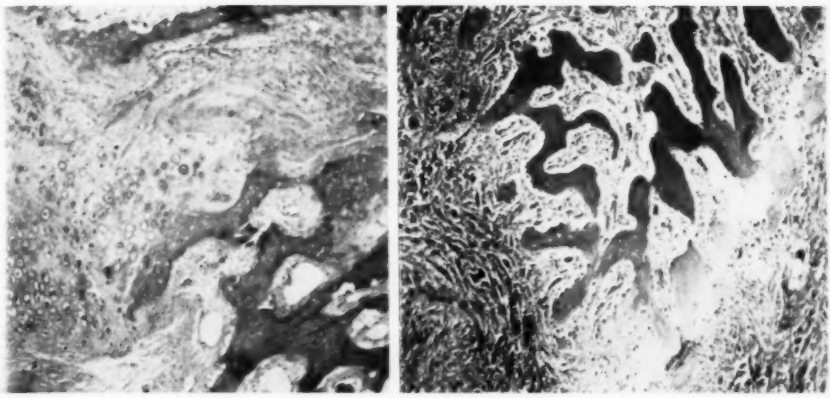
Fig. 4 a—b. Case 4. Parosteal sclerotic tumor encircling left tibia and fibula 3 years after onset of symptoms.

Case 3. Male, aged 32. Roentgen examination following an injury in 1948 (Fig. 3, a and b) revealed a tumor of the posterolateral supracondylar aspect of the left femur. The patient subsequently complained of pain and restriction of movement of the knee. Further roentgen examination four years later, in 1952, showed slight progression. The lesion was regarded as an osteoma, and partial excision was performed. The patient was admitted early in 1953; in spite of benign histologic appearances roentgenography indicated a progressive tendency of the tumor.

Mid-thigh amputation was performed four months later, after a course of preoperative roentgen irradiation with a tumor dose of approximately 4 800 r. There were no signs of metastases 6 years after amputation.

Roentgenograms in 1948 (Fig. 3, a and b) showed a broadbased, densely calcified mass adherent to the posterolateral supracondylar region of the left femur. There was no core of cancellous bone and no involvement of the medulla. No periosteal lipping or spicules were present.

Histology. Biopsy in 1952 (Fig. 3c) showed cellular connective tissue with osteoid and cart-



c d

Fig. 4 c—d. Case 4. c) Osseous and cartilaginous tissue resembling osteochondroma of moderate atypia. × 50. d) Amputation specimen. Highly differentiated osteogenic sarcoma. × 50.

laginous areas. The size of the nuclei varied considerably; few mitoses were present. Several sections were studied from the amputated specimen and great variations in different parts of the tumor, with intermingled areas of irregular bone, cartilage and fibrous tissues, were evident (Fig. 3d). The low cellularity may be due to irradiation. Diagnosis: osteogenic sarcoma of low malignancy.

Case 4. Male, aged 45, with vague pains in the left knee for 2 years, and a lump below the knee for a few months. Roentgen examination in 1952 revealed a tumor of the upper part of the left leg. The patient was admitted seven months later. Biopsy revealed only some signs of malignancy, and the tumor was regarded as being an osteochondroma. Six months later, roentgen examination showed progression and mid-thigh amputation was performed. No signs of metastases 6 years after amputation.

Roentgenograms on admission in 1953 (Fig. 4, a and b) showed a densely sclerotic tumor, partly encircling the upper parts of the left tibia and fibula. The periphery was irregular and less sclerotic than the central part of the tumor. No periosteal lipping or typical spicules were present.

Histology. Biopsy at the same time (Fig. 4c) showed areas of irregular bone spicules and cartilage of moderate cellularity. The chondrocytes exhibited moderate variation in size. Fig. 4d illustrates an area from the amputated specimen with irregular strands of bone and osteoid tissue in connective tissue with atypical spindle cells. Diagnosis: highly differentiated osteogenic sarcoma.

Case 5. Male, aged 30, with stiffness of the left knee of 3 weeks duration. On admission in 1955 roentgen examination revealed a tumor of the posterolateral region of the lower end of the left femur (Fig. 5, a and b). Histology showed only slight signs of malignancy and the growth was considered to be a fibro-chondro-osteoma. Two years later partial excision was performed. Roentgenography 2 years after the excision revealed progression, and in 1959 amputation of the lower third of the thigh was performed. No evidence of metastases on examination four months later.

a b

Fig. 5a—b. Case 5. Parosteal, irregularly outlined, sclerotic tumor of left lower femur 3 weeks after onset of symptoms.

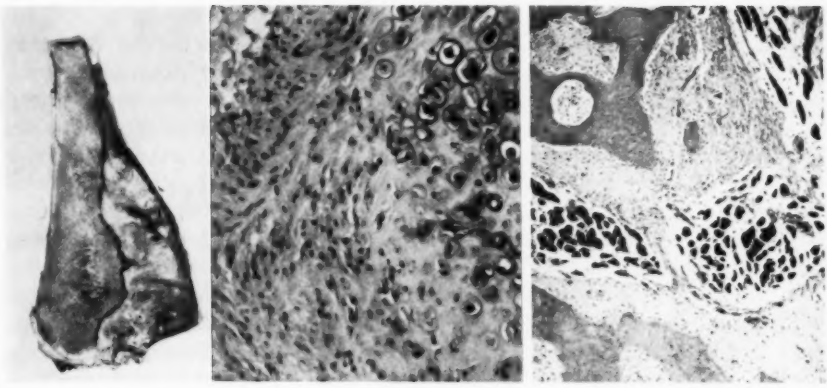
Roentgenograms on admission in 1955 showed a sclerotic tumor of the lower posterolateral aspect of the left femur, the periphery with a less dense, irregular, streaky appearance. No true spicules or periosteal lipping were evident (Fig. 5, a and b).

Microscopy. Biopsy in 1955 showed irregular strands of bone and osteoid tissue, and areas of cellular cartilage, partly embedded in osteoid tissue (Fig. 5d). The cells exhibited considerable variation in size and staining properties, the bone trabeculae being separated by fibrous tissue of fairly high cellularity. Histologic examination of the amputated specimen revealed osteoid and osseous trabeculae separated by fibroblastic tissue with atypical cells. Striated muscle was invaded (Fig. 5e). Diagnosis: osteogenic sarcoma of low malignancy.

Macroscopy. Examination of the amputated specimen demonstrated a parosteal tumor infiltrating the lower end of the femur; it had invaded the knee joint and partially destroyed the cartilage (Fig. 5c).

Discussion

The clinical course and the roentgenologic and histologic appearances in our 5 cases conform well with the accepted entity of parosteal osteogenic



c d e

Fig. 5c—e. Case 5. c) Amputation specimen. Parosteal tumor destroying and infiltrating left lower femur. Macroscopic intra-osseous extension demarcated. d) Cartilaginous and osteoid tissue of moderate atypia. × 125. e) Amputation specimen. Osteogenic sarcoma invading striated muscle. × 50.

sarcoma. The literature and our series bring the recorded cases of this lesion to 39 (COLEY and DWINNEL et coll., GESCHICKTER & COPELAND, and SAMMONS et coll.). A survey of these cases reveals certain distinct and peculiar features.

Sex and Age. There is no sex predominance (21 males and 18 females). As compared to the ordinary osteogenic sarcomas this type of growth occurs predominantly in older patients, 17 patients (44 per cent) being 30 years of age or more. The slow growth of the tumor may in part explain the higher age incidence; the tumor may have been of long standing before the onset of symptoms, as indicated by our Case 3.

Symptoms and Location. The duration of symptoms may extend over a period of months or years, 24 years in one case (DWINNEL et coll.). An indolent, occasionally tender, firm, and fixed swelling has been found clinically at the site of the lesion. In common with the ordinary osteogenic sarcomas, this tumor usually affects the metaphyseal region. In most cases (26 patients) the tumor arose in the supracondylar region of the femur as an indolent swelling interfering with the movements of the knee. More rare situations were the humerus (six cases), fibula (three), tibia (two), ulna (one), and radius (one case).

Roentgen appearances. The parosteal osteogenic sarcoma appears as a juxtacortical, broad-based, densely ossified mass, usually at the lower metaphysis

of the femur. The tumor is most sclerosed at its base. The less dense periphery is lobulated or irregular, but usually clearly defined. Within the tumor scattered rarefactions, corresponding to cartilaginous and fibrous areas or irregular cancellous bone may appear. The tumor is attached to the cortex along a part of its base, and characteristically tends to encircle the shaft; a clear zone of varying length may thus appear between the tumor and the bone. At the site of attachment the underlying cortex is usually thickened.

Periosteal lipping and spicules, typical of the ordinary osteogenic sarcomas are characteristically absent. The appearance of the tumor may remain unchanged for years. As progression ensues, cortical destruction and medullary invasion become evident, and separate ossified masses may appear in the adjacent soft tissues. These changes are particularly noticeable after an attempt at local excision. The recurrent tumor after local excision often appears at some stage much alike the primary growth (STEVENS et coll.).

Histology. The histologic appearances vary not only from lesion to lesion but also from one region to another within the same tumor. In typical cases the tumor consists of osteoid tissue and osseous trabeculae separated by sarcomatous connective tissue. Areas of more or less atypical cartilaginous tissue as well as purely fibrous zones are commonly seen. At the periphery, a capsule of fibrous tissue together with signs of invasion into striated muscle or fat tissue may be found. If the bone trabeculae are irregular and apparently formed of obviously sarcomatous connective tissue, the diagnosis is a simple one. When, however, the bone has a mature appearance, with quite well formed and regularly arranged trabeculae, and the connective tissue reveals only slight signs of malignancy, the diagnosis is difficult. In such cases the lesion is often under-rated, as it were, and regarded as being an osteoma or osteochondroma. Evidence of malignancy may, however, be present at least in scattered small foci. Multiple sections from the various parts of the tumor should be examined in dubious cases. It is therefore important that the pathologist is familiar with the peculiarities of this type of osteogenic sarcoma, is properly informed about the clinical signs and roentgenographic appearances, and is supplied with a sufficient amount of biopsy material. Recurrent tumors after incomplete removal have often been found to exhibit increased signs of malignancy.

Differential diagnosis

Myositis ossificans in most cases will be related to injury or paralysis. Roentgen examination shows laminated ossification along the fascial planes of the muscles; this increases rapidly for two to three months when its growth becomes stationary. Histology demonstrates bone spicules of cartilaginous or fibrous origin. Reactive fibrous tissue may be found between the bone trabeculae. The appearances may be mistaken for those of an osteogenic sarcoma of moderate malignancy.

The occasional development of sarcoma in myositis ossificans adds to the difficulty.

Ossifying subperiosteal hematoma may likewise present features very similar to parosteal osteogenic sarcoma and the microscopic differentiation may be extremely difficult. The history of adequate trauma may often indicate the true nature of this lesion. Roentgenologically, the lesion will soon attain its maximum and thereafter the subperiosteal hematoma will gradually assume a more orderly appearance and eventually persist as a cortical thickening.

Osteochondroma may have a broad base but does not tend to encircle the shaft. A core of cancellous tissue continuous with the medulla is usually seen. Scattered calcifications, as distinct from the dense ossification of the parosteal osteogenic sarcoma are characteristic. Histology shows a more orderly structure of cancellous bone, containing fatty or hematopoietic tissue. At operation, a peripheral cap of cartilage may usually be demonstrated. Development into a sarcoma may occur, but the sarcomatous tissue will mostly be of a cartilaginous nature.

Sclerotic osteogenic sarcoma is differentiated by its rapid growth, and by pain and systemic reactions. The films usually indicate a subcortical origin with medullary and cortical involvement. Periosteal lipping and spicules are often present. Histologically a bone-producing sarcoma is found throughout the tumor.

Treatment and Course

Of the 39 patients, 8 died after an average of 8 years (ranging from 4 to 18 years). One of these was primarily treated by irradiation and 7 by local excision. Twenty-one are reported alive after an average of 7 years (ranging from 1 to 15 years); 5 of these underwent primary amputation, while 16 had primary excision. No death is reported in the course of the first 3 years after the primary treatment. In 10 cases, death was due to other causes, or reliable information was not available.

A fairly common history of parosteal osteogenic sarcoma is that of an 'atypical osteochondroma', treated by excision and repeated surgical intervention for recurrence, perhaps leading ultimately to extensive metastases. The metastases may also show a slow growth rate, as indicated by our Case 1. The fact that the sarcomatous nature of this lesion may be found only in minor areas of the tumor makes the histologic diagnosis uncertain and the choice of treatment a difficult one. There is little evidence of radiotherapy being of any avail in these cases. Permanent cure by local excision of the tumor can be expected only in cases permitting radical extirpation with a fair margin of normal bone and soft tissue. Recurrence after local excision is extremely common (21 out of 30 primary excisions) and often in a more malignant form. Amputation should therefore be performed in cases of recurrence.

SUMMARY

Five cases of parosteal osteogenic sarcoma are reported, bringing the number of case published to 39. The roentgenographic and histologic appearances are described in detai and the differential diagnosis discussed; it is shown that this presents some difficulties. Th prognosis is often poor if radical treatment is not applied.

ZUSAMMENFASSUNG

Fünf Fälle von parostealem osteogenem Sarkom werden berichtet, wodurch sich die Anzah der publizierten Fälle auf 39 erhöht. Das röntgenologische und histologische Bild wird in Detail beschrieben und die Differentialdiagnose besprochen; es wird auf die diagnostische Schwierigkeiten hingewiesen. Die Prognose ist oft schlecht wenn keine Röntgenbestrahlun verabreicht wird.

RÉSUMÉ

Les auteurs présentent cinq cas de sarcome ostéogénique parostal, portant le nombr des cas publiés à 39. Ils en décrivent en détail les aspects radiologiques et histologiques e étudient le diagnostic différentiel; ils montrent que celui-ci présente quelques difficultés. Le pronostic est souvent mauvais si on n'applique pas un traitement radical.

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RELIABILITY OF PINHOLE METHODS IN EVALUATION OF RADIATION FROM EMISSION AREA IN ROENTGEN TUBES

by

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A device embodying the principle of the pinhole camera, consisting of a small hole in an absorbent plate placed between the source of radiation and the film, is generally used for obtaining roentgenograms of the focal spot and the off-focal radiation. From the films thus obtained the form, amount (4, 8), and relative intensity of the radiation from the different parts of the emission area may be studied (1, 2, 6, 7, 9). The pinhole camera, however, has definite sources of inaccuracy (5, 8) which have been studied geometrically. Much care is needed if accurate measurements, for instance of focal spot sizes, are to be made (8) and further errors may arise from the properties of the recording medium.

Some authors present conclusions regarding the intensity of the radiation from different parts of the focal spot and of the off-focal radiation. It has been stated that there should be an area of lesser radiation in the middle of the vigorous emission from the anode disc and that the location of this area should correspond with that of the focal spot during the rotation of the disc (7). Pinhole films showing stripes along the borders of the focal spot have been published (1), appearances stated to be caused by uneven radiation. In an image of a focal spot, which is moving along a film, an area of lesser intensity can be seen in the middle of the focal spot in some of the reproductions (3). In a study of the off-focal radiation, with ionization chambers and films as recording media, it is explained that the off-focal radiation may be more penetrating (harder) than the actual focal radiation (6). All these studies were based upon the pinhole principle.

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Fig. 1. Round pinhole films. a) Size of hole from 8 to 1.5 mm. An unsharp image is obtained. b) Smaller holes (1.0 to 0.7 mm), sharper images. The anode gives a double image which varies slightly in the different films.

Fig. 2. Enlarged image of the focal spot. Round hole of 0.7mm diameter. Distance from focus to hole 460 mm, from hole to film 5 540 mm. Reputed size of focal spot 1.2 mm. A double image of the focal spot is obtained.

If several pinhole films are obtained with one exposure, by using a series of pinholes of slightly different sizes, the image of the focal spot and the off-focal radiation changes from one to another (Fig. 1, a and b). With a large pinhole, an unsharp image is obtained (Fig. 1a) but as the size of the hole becomes smaller the image becomes better defined although at the same time the image of the anode disc shows a correspondingly uneven density (Fig. 1b); one gains the impression in examining the latter that it actually consists of two similar partially superimposed images. A pinhole film obtained with a

Fig. 3. Pinhole films obtained with a rectangular hole and with its longitudinal axis: perpendicular to the plane of the anode disc (a) and oblique to it (b). The 'marginal zones' of the focal spot (FRANTZELL) are different owing to the position of the hole.

Fig. 4. A large narrow slit has been used. An area of lesser density is present in the middle of the exposed strip (i. e. splitting of the image) when the slit is parallel or perpendicular to the anode disc.

shorter exposure produces an image only of the focal area. By suitable enlargement, i. e. by increasing the distance between the pinhole and the film, it is easy to produce a double image of the focal spot itself (Fig. 2). The pinholes used for the films in Figs 1 and 2 were round.

A 'splitting' of the image is liable to occur if the shape of the pinhole is altered. Fig. 3 shows films of a focal spot taken with a rectangular pinhole. The position of the pinhole in relation to the focal spot has been changed for the different films. The splitting is most clearly seen if the optical axis of the pinhole lies at right angles to the plane of the anode disc, but reasonably well even when the axis of the hole and the plane of the disc are parallel. Oblique positions produce different images. Distortion of the image was demonstrated in all possible positions of the pinhole. A large narrow slit of infinite longitude gives an image in the middle of which an area of lesser density is present (Fig. 4). A pinhole of triangular shape produces a triangular image, the apices of which are split. Pinholes of irregular shape produce the same phenomena of uneven density and distortion of the image (Fig. 5).

The various appearances described seem to correspond to those reported by FRANTZELL (1), JANKER (3), and MATTSSON (7). The recognized fact that the true focal spot is not a square but a rectangular, relatively narrow area, which is obliquely situated in relation to the optical axis of the pinhole camera, lends support to the theory that 'optical' errors are likely in such a system. The obliquity is evidently partially responsible for the distortion of the images.

The purpose of this communication is to show that markedly different intensity distribution, apparent in the degree of blackening of the film and dependent upon the size, shape, and position of the pinhole, may be observed in these investigations. The films cannot be wholly relied upon in the evaluation of the radiation of the different parts of the emission area. The film gives a true representation of the beam of radiation between it and the pinhole and the same holds true for all pinhole methods regardless of the recording device.

Fig. 5. Irregular pinholes produce uneven images of the focal spot.

This is not meant to deny the possibility of an uneven emission of radiation It only indicates that any unevenness demonstrated is not necessarily o significance if the inherent characteristics of the pinhole camera are ignored

Acknowledgement

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SUMMARY

The effect of changes in the shape, size, and position of the pinhole upon the images of th focal area and off-focal radiation is described and discussed with reference to a series of ex perimental roentgenograms. It is shown that pinhole films are not necessarily reliable as means of evaluating the radiation given off from the various parts of the emission area.

ZUSAMMENFASSUNG

Es wird der Effekt der Form-, Grössen- und Lageänderung der Lochblende auf die Ab bildung des Fokus und der fokusfernen Strahlung beschrieben und an Hand einer Serie vo experimentellen Radiogrammen besprochen. Es wird gezeigt, dass Lochblendenfilme nich zuverlässlich sind, wenn es gilt die Strahlung zu ermitteln die von den verschiedenen Teile der Strahlenquelle ausgesandt wird.

RÉSUMÉ

En se basant sur une série de radiographies expérimentales, l'auteur décrit et étudi l'effet des modifications de forme, de dimensions et de position du trou d'épingle sur les image de la surface focale et du rayonnement extra-focal. Il montre que les films obtenus avec u trou d'épingle ne sont pas toujours un moyen fidèle d'évaluer le rayonnement provenan des différentes parties de la surface émettrice.

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A COMPLICATION IN COBALT BEAD TREATMENT OF CANCER OF THE BLADDER

Report of a case

by

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Radiocobalt in bead form (1, 2, 3) has been employed since 1951 for contact radiation in suitable cases of bladder tumours (1, 4). The aim is usually to arrange the beads spherically in the bladder as close as possible to the tumour; on conclusion of the irradiation the beads are pulled out through the urethra by means of the silk thread on which they are strung.

No complications due to this method appear to have been reported and the publication of a case in which they occurred may therefore prove of interest.

Case report

A farmer, aged 60, had suffered for six months from occasional hematuria, dysuria and back pain, and was admitted in March 1958. Biopsy disclosed epidermal papillomatous carcinoma of the bladder. Because of the site and the large size of the tumour its excision was not considered possible and transurethral electrocoagulation was performed twice, after which the patient was referred for treatment to the radiotherapy department.

The patient over seven months received 6 000 r telecobalt treatment, 8 500 r roentgen sieve treatment, and one cobalt bead treatment totalling 3 000 r, 25 active Co ^{60} beads and 20 inactive beads being inserted, strung in a 47 cm row, transurethrally into the bladder by means of the applicator devised by BECKER and SCHEER (1). The beads were 6 mm in diameter, and the active beads were threaded on alternately with the inactive beads.

Three months after the last treatment it was shown by cystoscopy that the tumour had progressed and extended from the internal urethral meatus to both ureteral orifices, which it surrounded. The tumour thus occupied the whole trigonum and even a part of the bladder roof. It was decided to continue the cobalt bead therapy. The second treatment, which was similar to the first, was uneventful, but five days later the string of beads could

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Fig. 1. The knot formed by the cobalt beads held up in the region of the pars cavernosa of the urethra, and the end of the string of beads in the distal part of the urethra. Penis vertical.

not be removed from the bladder. It was found that the end of the string of beads was held up in the prostatic part of the urethra and could not be pushed back into the bladder. Spinal anaesthesia was induced. On rectal examination the end of the string of beads seemed to be about 2 cm in diameter. In view of the fact that the patient had received so much external irradiation to the region of the bladder that healing of a cystotomy wound seemed doubtful, and that the diameter of enlarged end of the string of beads was of such an order as seemed to allow removal by the transurethral route without major trauma, it was decided to attempt removal by traction once more. The string now passed fairly easily through the pars prostatae, but its end was held up in the proximal portion of the pars cavernosa. Eight beads, which were now outside the urethra, were removed. Roentgenographic examination showed that there was a knot at the enlarged end of the string (Figs 1 and 2) which had evidently formed inside the bladder. On increasing the pull slightly the thread broke close to the knot, and ten active and ten inactive beads were slowly pulled out. On palpating the knot in the region of the pars cavernosa, it was felt suddenly to open. A finger was now quickly placed on the last palpable bead to prevent the others falling back into the bladder and seventeen more beads were slowly extracted. The silk thread inside the urethra was gripped with atraumatic intestinal forceps and, together with the last two beads, extracted.

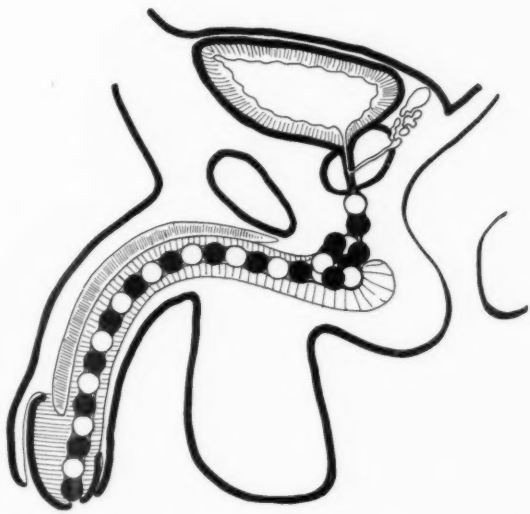

Fig. 2. Schematic drawing of urogenital region in the sagittal plane showing the site of the knot in the proximal part of the pars cavernosa.

The beads had remained in the body 5 hours and 20 minutes (in the urethra 2 hours) longer than had been calculated. It was estimated that the urethra received about 500 r and the bladder a total of 4 094 r, or 1 094 r more than originally planned. The gamma activity of one bead is about 5 mC (1).

A catheter (Nelaton No. 20) was inserted for three weeks, and a course of nitrofurazone was given to prevent infection. The patient made an uninterrupted recovery. Examination 4.5 months later, however, showed the formation of a stricture in the proximal part of the pars cavernosa. It was found possible to introduce a Nelaton No. 10 catheter and, after bougienage, a Nelaton No. 16 indwelling catheter into the urethra. The patient complained of pain in the lower abdomen, dysuria and hematuria. Urography revealed bilateral hydronephrosis and hydroureter. The capacity of the bladder was only 50 ml. The nonprotein nitrogen was 38 mg, which increased to 60 mg in about a month.

It was evident that the urethral stricture did not essentially affect the patient's condition, but the bladder carcinoma tended to obstruct the ureters. Uretero-ileocutaneostomy was therefore performed and disclosed metastases. The patient died four days after the operation of paralytic ileus.

Discussion

The case described shows that cobalt bead therapy for bladder carcinoma may be associated with a risk of complications. In this case a large loop had probably formed in the string at some stage and an end of the string had slipped through the loop, resulting in an open knot at the middle of the string.

When an attempt was made to pull out the beads, the knot had tightened and slipped to the end of the string. One possibility to prevent a complication of this kind would, of course, be to thread the beads very close together so that the stiffness of the string would prevent loop formation, but as the beads cannot then be arranged in a spherical fashion, homogenous irradiation would not be obtained and the main principle of the therapy would suffer.

If this complication occurs, cystotomy and transvesical removal of the beads are obviously the safest therapeutic measures. Unfortunately, however, the patient has often received so much external irradiation of the lower abdomen that healing of an operation wound may be doubtful. In certain cases the string of beads may be successfully pulled out through the urethra, although damage to the latter both from trauma and irradiation is then always possible, as happened in our case.

SUMMARY

An unusual complication which occurred in connection with cobalt bead therapy for bladder carcinoma is described. When an attempt was made to remove the string of cobalt beads a knot was formed; the beads were eventually removed by the transurethral route after the thread had broken off close to the knot, which then opened spontaneously.

ZUSAMMENFASSUNG

Eine ungewöhnliche Komplikation im Zusammenhang mit Kobaltperlen-Therapie bei Blasenkrebs wird beschrieben. Beim Versuch, die Kobaltperlenkette zu entfernen, formte sich ein Knoten. Die Perlen wurden schliesslich, nachdem der Faden nahe dem Knoten, der sich dann spontan öffnete, abgerissen war, auf transurethralem Wege entfernt.

RÉSUMÉ

Les auteurs décrivent une complication inhabituelle survenue au cours d'un traitement par des perles de cobalt pour un cancer de la vessie. Quand on essaya de retirer le chapelet de perles de cobalt, il se fit un nœud. Les perles furent finalement retirées par voie urétrale, après que le fil se fut rompu près du nœud, qui se défit alors spontanément.

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RESPIRATORY KYMOGRAPHY IN ACUTE ABDOMINAL CONDITIONS

by

SAM SCHMIDT

Respiratory movements are of two main kinds, diaphragmatic and costal. Both these movements are influenced by the condition of the lungs and pleurae as well as by that of the abdominal organs and walls. Fluoroscopy can give a general idea of the diaphragmatic excursions but scarcely more. Roentgenkymography on the other hand, offers a more accurate and objective analysis of the respiratory movements. The aim of the present paper is to report on the results of kymographic investigation of the diaphragmatic and costal movements in various acute abdominal conditions.

Roentgen kymography of the respiratory movements has been studied by several authors although the investigations have been confined to the measurement of amplitude and the diagnosis of diaphragmatic paralysis. The first communication came from STUMPF in 1931. DAHM (1932 and 1933) reported the application and results of kymography in chest examinations. He studied normal and pathologic movements of the ribs and diaphragm and observed reduced diaphragmatic excursions in conditions such as cholangitis, subphrenic abscess, and perinephritic abscess, associated with peritoneal irritation. He did not, however, analyse or describe the kymographic waves obtained. He concludes (1933) that by considering the numerous possibilities

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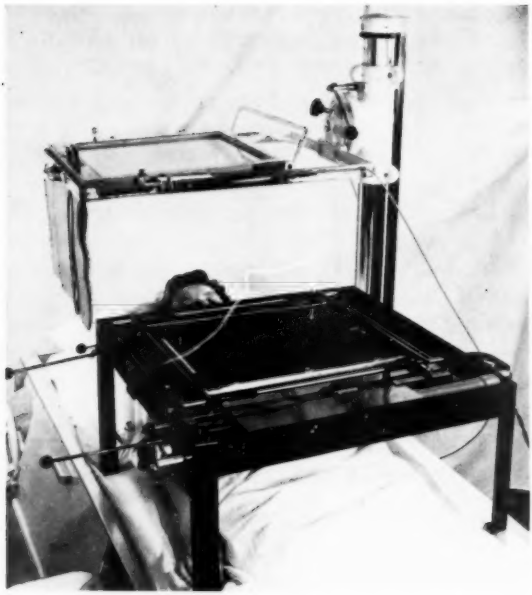

Fig. 1. The kymograph on the examination table placed over the chest of a patient.

of movement of the diaphragm in breathing, and the different factors which create and influence these movements, one can hardly expect a consistent typical movement pattern in a given disease.

WEBER (1933 and 1934) published kymographic studies of the respiratory mechanics. EPSTEIN (1955) reported 250 diaphragm kymographies (100 normal and 150 pathologic cases); out of 12 cases of subphrenic abscess he found complete paralysis in 3 cases and in a further 9 cases there was moderate restriction of movement together with variable slight blunting of the apex of the waves and a slight lag of the onset of the expiration wave. In postoperative cases of gastrectomy and cholecystectomy he found slight or moderate restriction of movement of the diaphragm. The same author warns against placing too much accuracy upon the evaluation of postoperative roentgenkymograms. In emphysema, basal pleurisy, pneumonia, atelectasis, and pulmonary and mediastinal neoplasms his findings were that the movements of the diaphragm persist in a relatively normal pattern.

EPSTEIN made his examinations in ordinary breathing and the exposure time was 3 seconds. He performed no kymographic studies in deep breathing.

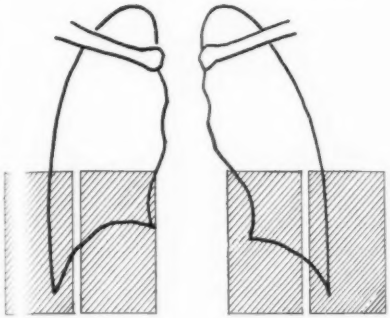

Fig. 2. Schematic drawing showing the two lead plates with slits in position over the lower part of the chest.

We have not been able to find any record of a study of kymography of the diaphragm and ribs in deep breathing, nor have we come across any systematic study of the wave form in various abdominal and thoracic conditions.

Technique

The kymograph is supported on legs 35 cm in height, and is fitted with two movable lead plates with a 1 mm wide slit in each; above these plates lies the moving tray to hold the cassette. Each plate is placed over one side of the diaphragm and lower half of the chest under fluoroscopic control so that the slit lies parallel to the long axis of the body and about 2 to 4 cm medial to the lateral thoracic wall; it also lies lateral to the heart whenever possible. During the exposure the tray with the cassette travels for a distance of 5.5 cm from the right to the left. We thus obtain a record of movement of a one millimetre broad segment of the diaphragm and the lower half of the chest on each side (from about the 7th to the 10th ribs).

The roentgen beam is centered over the spine under fluoroscopy control and is limited laterally to include the thoracic wall on each side, and vertically about 10 to 12 cm above and below the diaphragm. Both sides are exposed simultaneously on the same 30 × 40 cm film placed transversely. Exposure factors: 90 to 110 kV, 10 mA, and 20 seconds. The relatively long exposure time is necessary in order to record at least 2 or 3 respiratory cycles in deep breathing. Two films are exposed, one during ordinary and one during deep respiration. The patients were examined in the supine position with the roentgen tube below the table; this makes it possible to examine abdominal cases in the same position as other cases and, in addition, the position eliminates body movements during respiration. The entire examination takes about 6 minutes.

Two-slit kymograph combined with a long exposure time produces good film quality with sharply defined wave-tracings and well defined right and left fields, which are easy to examine and compare with each other.

We are conscious of the fact that different parts of the diaphragm and ribs normally have different amplitudes and possibly different movement patterns. However, by examining all the patients under similar conditions, the records obtained are comparable and pathologic tracings can be distinguished from the normal. Another possible objection is that the movement of the lateral parts of the diaphragm and ribs, which are recorded, are not in the direction of the slits but lie more or less obliquely to them. Regarding this, McLaren (1948) stated: A true graphic picture of movement is recorded only when the movement is in the direction of grid slits, but clinical experience and interpretation allow for analysis and diagnosis of movement not taking place quite in the line of the slit. This also applies to the slight difference between the real amplitude and apparent amplitude as measured in the film.

Material

Respiratory kymography was carried out with the technique described in 500 cases, 87 of which were acute abdominal cases. The examination was also carried out in 30 normal cases, as control material. Only the normal and the abdominal cases are dealt with in this paper, thus 117 cases in all, as defined below:

	Cases
Normal control cases	30
Subphrenic abscess	9
Multiple liver abscesses	2
Postoperative abdominal haemorrhage	1
Acute small intestine ileus	10
» cholecystitis	11
» pancreatitis	5
Perforated duodenal ulcer	5
» appendix (and acute appendicitis)	4
Other acute abdominal conditions such as gastroenteritis and abdominal pain of unknown origin	40
Total	117

The above classification was made after clinical and/or roentgenologic diagnosis and verified in many cases by operation. In several cases the diagnosis was first suggested by the results of kymographic examination. The control

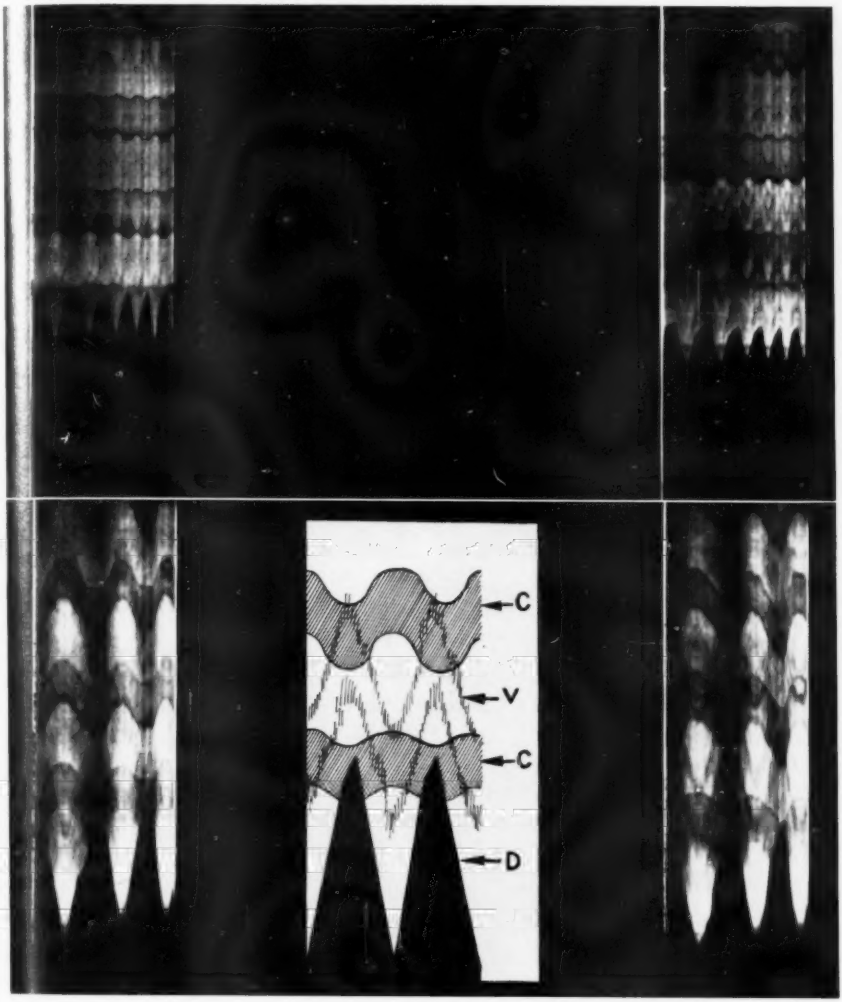

Fig 3. Normal kymographic appearances, in ordinary respiration (upper tracing) and in deep breathing (lower tracing). A schematic drawing is placed between the tracings of the right and left sides in the lower tracing. D — Diaphragmatic movement wave, C — Costal movement wave, V — Movement wave of a pulmonary vessel.

cases were healthy individuals undergoing routine lung examination. The age of the patients varied from 20 to 79 years. The length of the case history was 6 hours to several months, the average being a few days.

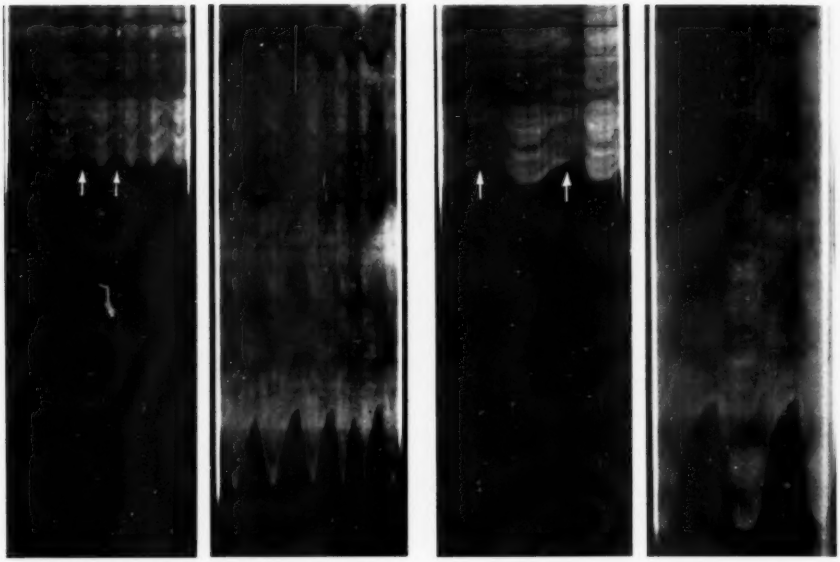

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Fig. 4. Right subphrenic abscess two weeks after cholecystectomy. Plateau-shaped diaphragmatic waves (↑) with considerable reduction of diaphragmatic and costal amplitude on the right side in both ordinary (a) and deep breathing (b).

Results

In Fig. 3, reproductions of the original 30 × 40 cm films are shown. In the subsequent illustrations, the tracings of the right and left sides are placed close to each other in order to save space.

Normal respiratory kymographic appearances

Each film shows two exposed areas representing the right and the left side of the chest respectively.

The tracing of the normal *diaphragmatic movements* consisted of a number of asymmetric steep waves. The ascending, expiratory limb was straight in its lower two thirds and slightly curved in its upper third, indicating some slowing down towards the end of expiration. The descending, inspiratory limb formed a straight line. The apex of the wave, the transition from expiration to in-

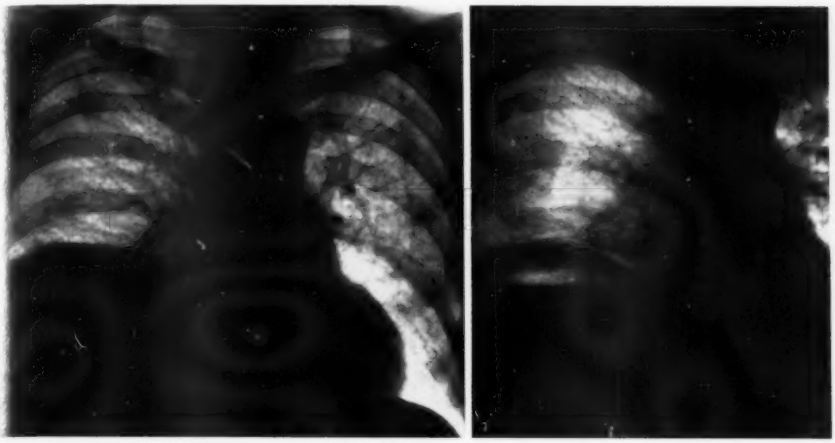

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Fig. 5. Same case as in fig. 4. a) Chest film taken at the same time as kymography was performed. b) Two weeks later: large subphrenic abscess.

spiration, was a sharp-pointed angle. This shows that there is normally no appreciable interval between expiration and inspiration. The lowest part of the wave, i. e. the transition between inspiration and expiration was most often a sharp angle, though sometimes slightly rounded, especially in deep breathing. The amplitude varied with the type of respiration, the age and possibly the constitution of the individual. The average was 2 cm in ordinary and 4.5 cm in deep breathing.

The *rib movements* showed an opposite direction to the diaphragmatic excursions. The movements of the posterior lateral parts of the ribs were recorded but sometimes even those of the anterior parts of the ribs were visible. The ribs generally showed a slight undulating wave, but in some cases the transition between inspiration and expiration was a pointed angle similar to the diaphragmatic tracing. The amplitude was on an average 1 to 2 mm in ordinary and 5 mm in deep respiration.

The diaphragmatic and costal movements were synchronous and similar on both sides as regards the configuration, amplitude, and frequency of the waves. There occurred, however, a slight difference in amplitude between the two sides in the diaphragmatic movements (up to 0.5 cm) and to an even greater degree in the costal movements.

Respiratory kymographic appearances in acute abdominal cases

The respiratory kymographic waves showed changes in form, amplitude or direction in acute abdominal conditions, the changes being unilateral o bilateral. It should be stated that there was in some cases a relationshi between the thoracic and diaphragmatic respiration with a compensator mechanism. In cases with reduced diaphragmatic excursions there was ofte a compensatory increase in the respiratory costal movements. This compensa tion when present was usually observed on the contralateral side. On th other hand a low respiratory amplitude was often compensated by an increase frequency.

In our experience diaphragmatic paralysis with paradoxical movement is difficult or even impossible to recognize by fluoroscopy. This, on the othe hand, was easy in the kymogram and could be done in two ways: (1) b observing the direction of the diaphragmatic movements in relation to th rib movements, and (2) by comparing the diaphragmatic waves on the affected side with those on the opposite side and measuring the respective distance between the apices of the waves on each side and noticing their direction.

I. *Subphrenic abscess.* Nine cases, all but two of the postoperative type. All were diagnosed roentgenologically and clinically. One was operated upon. Length of histories: one to four weeks.

In seven of these cases the diaphragmatic movement wave on the affected side showed a considerably reduced amplitude (3 to 12 mm) with a blunted, horizontal or slightly oblique apex, i. e. transition between expiration and inspiration. This 'plateau' wave appeared in the deep breathing tracing in six cases, and in ordinary breathing in one case. The diaphragmatic wave on the healthy side was normally shaped with a slightly or moderately reduced amplitude. In two of the nine cases there was diaphragmatic paralysis with paradoxical movement and low amplitude (2 to 4 mm) on the side of the abscess. On the contralateral side in these two cases the wave was normal in shape but the amplitude slightly reduced.

In all the cases the amplitude of the rib movements was slightly or moderately reduced on the affected side and was average or increased on the other side. In two of the cases even the rib movements on the affected side showed a typical plateau-shaped wave facing the diaphragmatic plateau.

II. Two cases of *multiple liver abscesses* of several months duration: one verified by operation and one at postmortem examination. One had a plateau-shaped diaphragmatic wave with reduced amplitude on the right side, and the other on both sides. Both cases showed restricted rib movements and one of them a plateau wave.

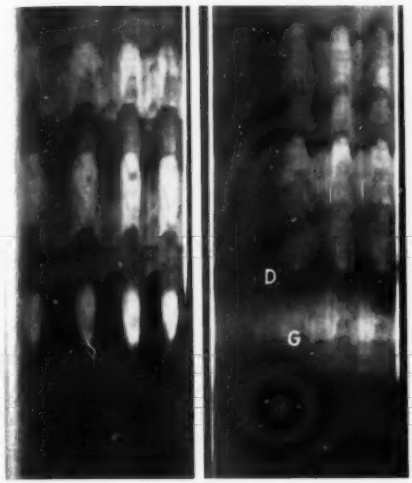

Fig. 6. Left subphrenic abscess caused by perforated diverticula of colon. One month's history. Deep breathing kymogram. D — Left side of diaphragm showing plateau waves with low amplitude. G — Gas in abscess cavity.

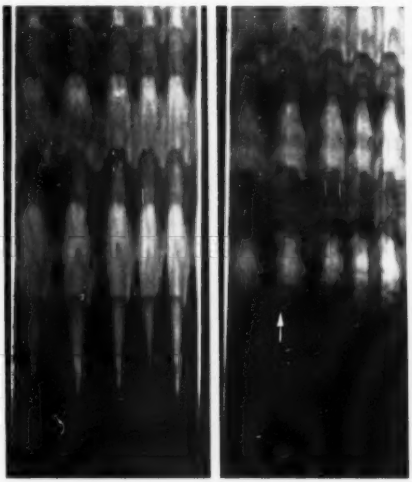

Fig. 7. Same case, 4 months later. The abscess has been drained. Deep breathing kymogram. Left side of diaphragm shows small paradoxical movements (↑).

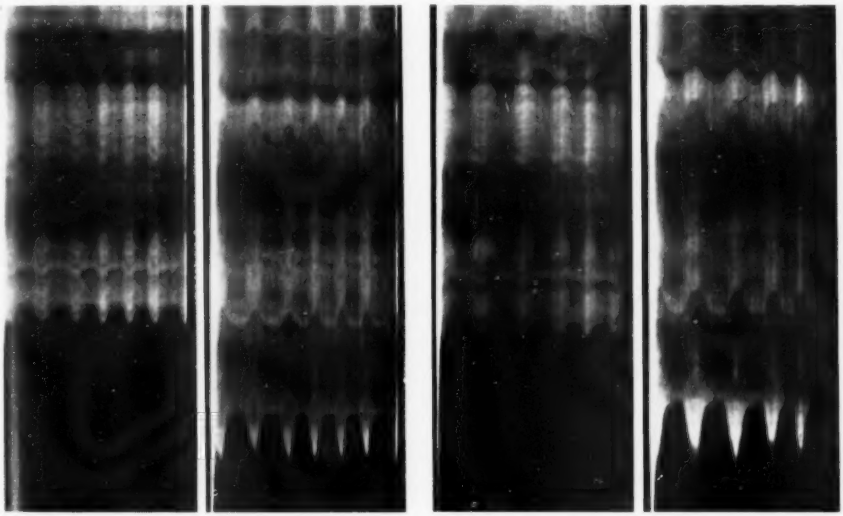

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Fig. 8. Three weeks after cholecystectomy two litres of blood found, mostly under the right side of the diaphragm, at operation. (a) Ordinary, and (b) deep breathing kymogram. Plateau-shaped diaphragmatic waves on both sides with considerable reduction of amplitudes, particularly on the right. Plateau waves in costal movements on the right side.

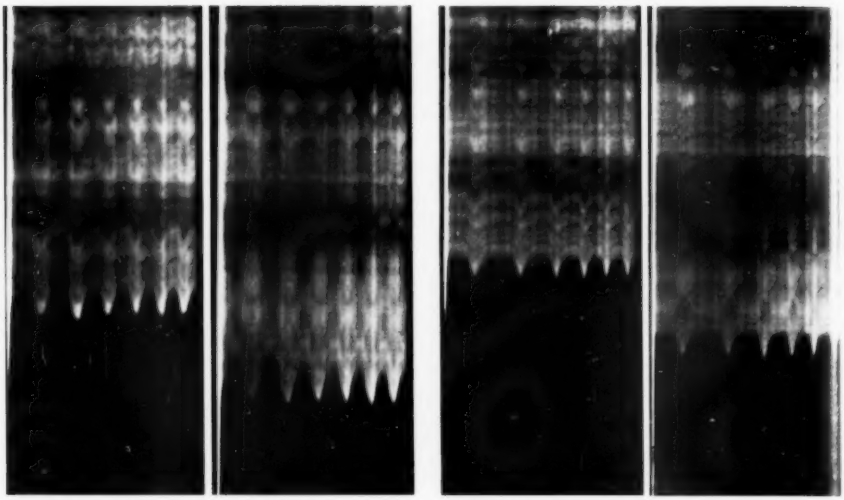

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Fig. 9. Ileus with peritonitis caused by perforating tumor in sigmoid colon. Three days history. a) Ordinary, and b) deep respiration kymogram. The last shows diaphragmatic plateau with considerably reduced amplitude on both sides.

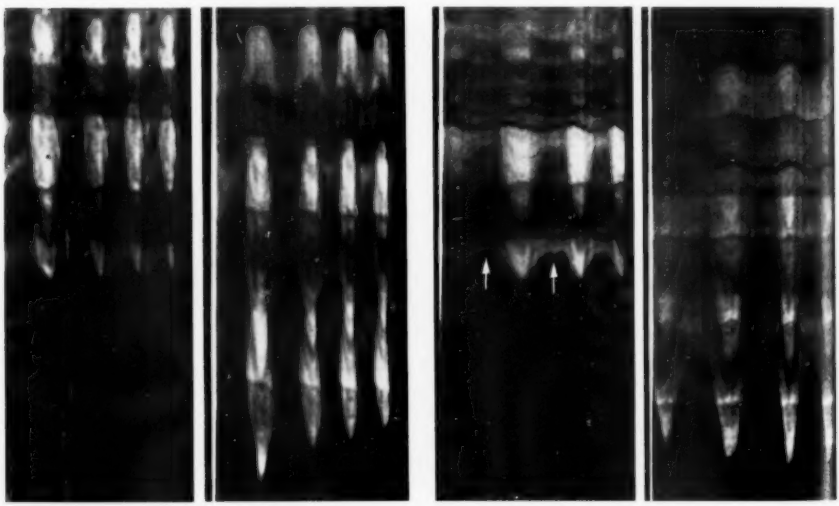

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Fig. 10. Acute cholecystitis. Five days history. Diaphragmatic plateau with marked reduction of costal and diaphragmatic amplitude on right side. a) Ordinary breathing, b) The plateau waves (↑) appear in the deep breathing kymogram.

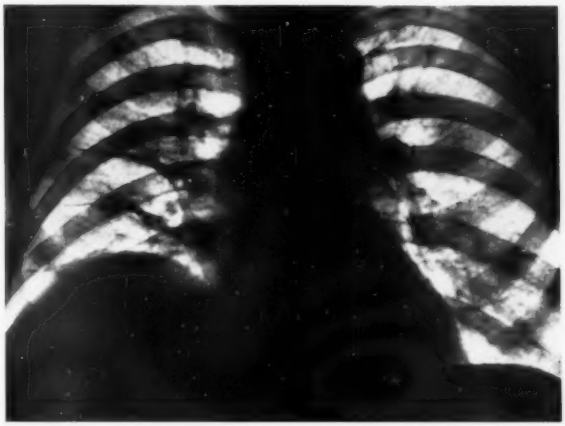

Fig. 11. Chest film in same case as in fig. 10. Raised right side of diaphragm with minor atelectasis.

III. One case of *severe abdominal haemorrhage* three weeks after cholecystectomy. (At operation two litres of partly coagulated blood, the greater part of which was found under the right diaphragm, was removed.) Kymographic findings: Diaphragmatic plateau waves of very low amplitude (3 mm) on the right side and oblique plateau of slightly greater amplitude (10 mm) on the left side. The ribs showed plateau waves of low amplitude. The respiratory frequency was high.

IV. Ten cases of *acute ileus* with a history of 6 hours to four days duration. All were diagnosed clinically and roentgenologically, and 7 were operated upon. Six of these cases had plateau-shaped diaphragmatic waves on both sides, with reduced diaphragmatic and costal amplitude in 4. The plateau was present in the deep breathing tracing in these 4 cases which were operated upon and an effusion was found in the peritoneal cavity; 2 of them had plateau-shaped costal waves.

In 2 cases, the plateau appeared in ordinary breathing only and there was an average respiratory amplitude. Both these cases resolved spontaneously.

Three ileus cases showed normal diaphragmatic waves and amplitude on both sides; there was reduced rib movements in 2 and paradoxical movements in one. One case with a four days history, and which on operation was found to have adhesions with a peritoneal effusion, had small bilateral paradoxical diaphragmatic movements and restricted costal respiration.

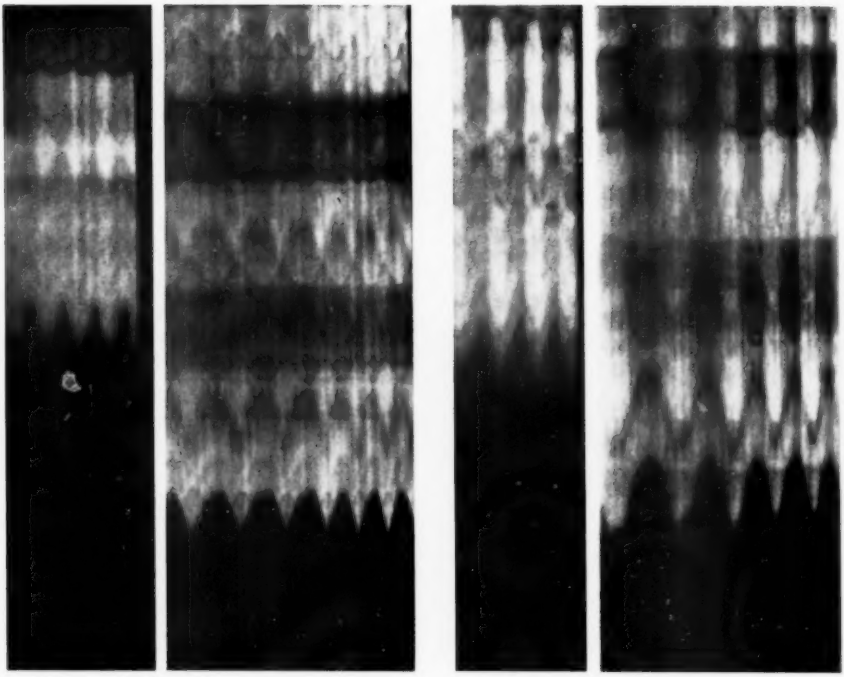

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Fig. 12. Acute pancreatitis. Four days history. Marked reduction of diaphragmatic amplitude bilaterally with plateau wave on left side in the ordinary breathing kymogram (a). Deep breathing tracing in (b).

V. There were eleven cases of *acute cholecystitis*, all diagnosed clinically and with positive roentgenologic findings. The duration of the histories ranged from twelve hours to seven days. All the cases showed moderate to considerable reduction of diaphragmatic amplitude on the right side, and all but three a reduction of the costal amplitude on the same side. Six of the cases had plateau-shaped diaphragmatic waves on the right side, five in the deep breathing and one in the ordinary respiration tracing. One of them showed plateau waves in the costal movements. Five cases had ordinary or step-formed diaphragmatic waves on the right side, and one of these cases had a plateau tracing on the left side with marked reduction in the amplitude, suggesting pancreatitis. Of the other left side tracings, five showed ordinary or step-like

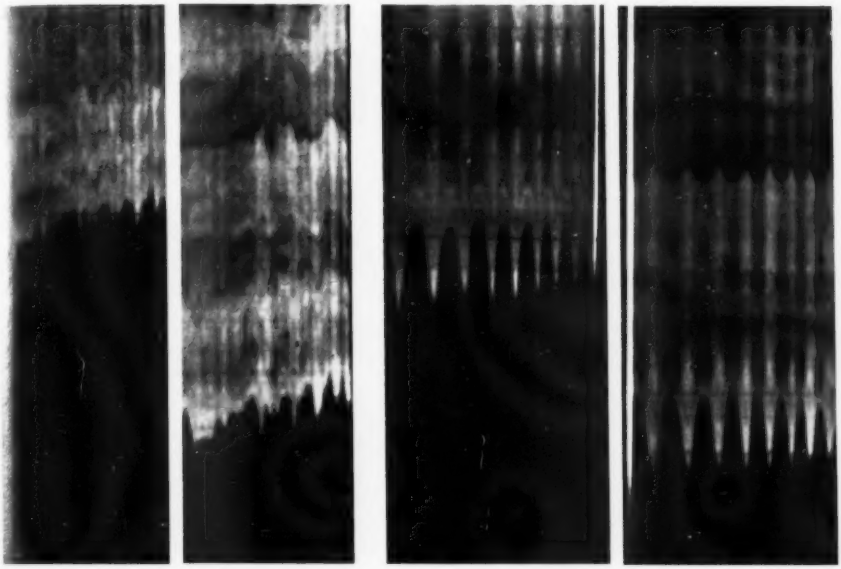

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Fig. 13. Perforated duodenal ulcer. About 12 hours history. a) Ordinary breathing. Irregular and rapid respiratory movements. b) Deep breathing. The respiration has become regular. Markedly reduced diaphragmatic amplitude with normal wave form bilaterally. Reduced costal amplitude on right side.

diaphragmatic waves with moderately reduced amplitude, and five cases a normal amplitude. The costal amplitude on the left side was normal or slightly reduced.

VI. Five cases of *acute pancreatitis* diagnosed clinically and by roentgenologic and laboratory findings, with a history of from three to seven days. All of them showed a plateau-shaped diaphragmatic wave on the left side with markedly reduced amplitude on both sides (except for one patient with normal amplitude on the right side). The right cupola of the diaphragm presented normal, step-formed, or oblique plateau-shaped waves. Four of the cases had moderately reduced costal respiration amplitude on the left side, and three of these showed a plateau-shaped costal wave. On the right side the costal amplitude was normal in two cases and reduced in three.

VII. A group consisting of five cases of *perforated duodenal ulcer*, two of *perforated appendix* with abscess formation, and two cases of *acute appendicitis*.

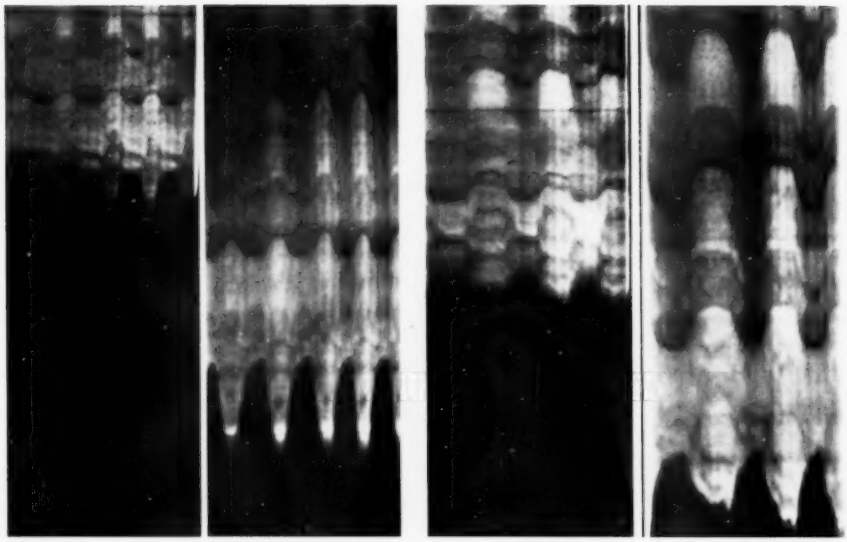

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Fig. 14. Same case as in fig. 13. Right subphrenic abscess 2 weeks after operation. a) Ordinary. b) deep breathing. Diaphragmatic plateau wave with considerably reduced amplitude on the right side in both tracings. Moderately reduced diaphragmatic amplitude on left side with compensatory increase of costal amplitude. Costal plateau waves.

The duration of the histories varied from one day to three weeks. The diaphragmatic movements showed moderate to considerable bilateral reduction of amplitude with normal, irregular or step-formed diaphragmatic waves on both sides. Only in one case of an appendix which had perforated a few days previously, did the diaphragmatic movements on the right side show oblique plateau waves.

The costal respiration amplitude on the right side was reduced in six cases, normal in two, and increased in one. On the left side it was reduced in four, normal in four and increased in one case.

VIII. Forty cases of *acute abdominal pain of unknown origin*, some of them diagnosed as gastroenteritis or a similar condition, were examined by kymography. All these cases completely recovered in one to three days; none was operated upon. All of them showed bilaterally normally formed diaphragmatic respiratory waves; about half (21 cases) had average diaphragmatic and costal amplitudes. There was slightly or moderately reduced diaphragmatic

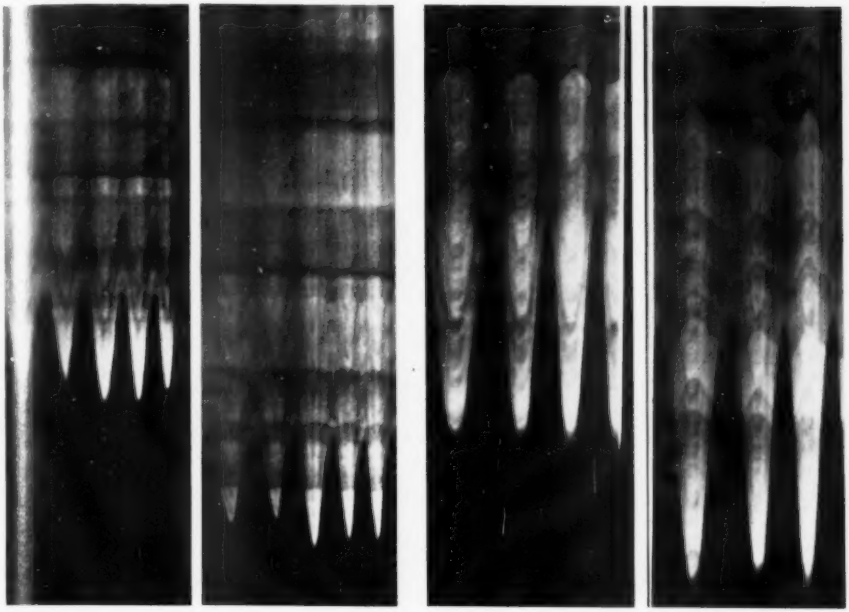

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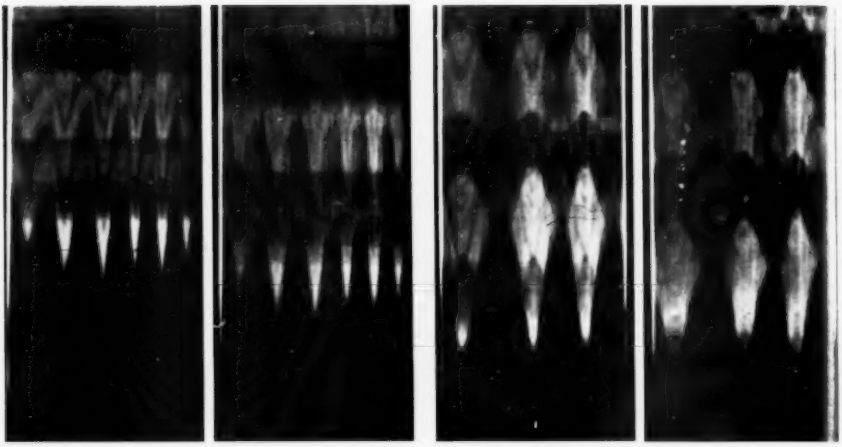
Fig. 15. Same case as in figs 13 and 14, 6 months later. Now symptom-free. Normal form and amplitude of diaphragmatic and costal waves. a) Ordinary, and b) deep breathing kymogram.

amplitude in 17 cases with normal, reduced or increased costal amplitude in approximately equal proportions. Two cases showed a considerable reduction in diaphragmatic and costal amplitude.

Discussion

As stated earlier, two films are exposed, one during ordinary respiration and one during deep breathing, in each one of our kymographic examinations. The two tracings are complementary. The first records the patients' ordinary spontaneous respiration. The second may be considered as a functional test; it often shows a pattern different from the one obtained with ordinary breathing and may afford important diagnostic information.

A *plateau-shaped diaphragmatic wave* was found in 6 out of 9 cases of subphrenic abscess, in the 2 cases of multiple liver abscesses, in the case of severe postoperative abdominal haemorrhage, in 6 out of the 11 cases of acute



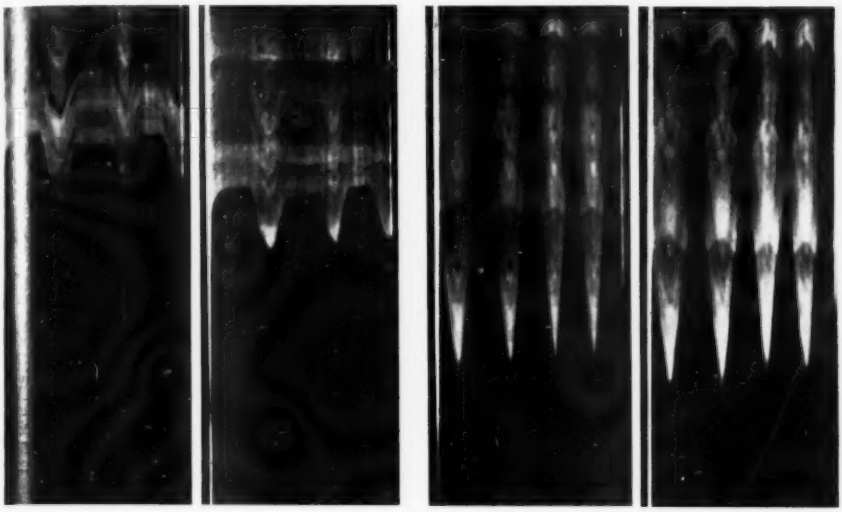
a b

Fig. 16. Case of acute abdominal pain of unknown origin. Negative clinical and roentgenologic findings. Normal kymographic appearances both in ordinary (a) and in deep breathing kymogram (b).

cholecystitis, in the 5 cases of acute pancreatitis and in 6 out of the 10 cases of acute ileus. The plateau wave was as a rule present on the affected side only. This finding would thus very frequently appear in inflammatory conditions in the immediate proximity of the diaphragm, or in organs with intimate lymphatic connections with the diaphragm. The plateau was present on both sides in the ileus cases and appeared in the more severe cases which on operation had a peritoneal effusion. No plateau wave was found in the seven cases with visceral perforation. This seems contradictory and further investigations of similar cases are required. None of the forty cases of acute abdominal pain without definite clinical or roentgenologic signs showed a plateau wave.

The plateau wave represents a short apnoeic period at the end of expiration. This apnoea may be explained by a standstill of the diaphragm, a reflex defence against compression of the inflamed peritoneum during the approaching inspiratory phase. It is a reflex mechanism similar to the one guarding the abdominal muscles during palpation. This mechanism would also explain why the plateau wave usually appears in deep breathing when the inspiratory pressure of the diaphragm increases.

The *diaphragmatic amplitude* was reduced in all but six of the severe abdominal cases. The degree of movement restriction was moderate to considerable but always more marked on the affected side in localized conditions. About half



a b

Fig. 17. Case with signs of mild ileus. No delay in passage of barium through small intestine. Symptom-free 6 hours later. a) Ordinary breathing: plateau-shaped diaphragmatic waves with normal amplitude. b) Deep breathing: normal wave form and amplitude of diaphragm and ribs. This patient probably held his breath after each expiration during ordinary breathing.

of the cases of abdominal pain of unknown origin had slightly or moderately reduced diaphragmatic amplitude. There seems to exist a relationship between the degree of restriction of the diaphragmatic movements and the severity of the abdominal signs, a plateau wave appearing in the more severe cases.

Diaphragmatic paralysis as shown by paradoxical movements was relatively rare: it was found only in two cases of subphrenic abscess and in one ileus case. (In EPSTEIN's material it was present in three out of twelve cases of subphrenic abscess.) Diaphragmatic paralysis is probably caused by direct extension of infection to the diaphragm, and not only by reflex guarding. Its late occurrence and relative frequency in subphrenic abscess supports this view.

Costal respiration was slightly or moderately restricted on the affected side in the majority of the severe cases. There was often compensatory increase of amplitude on the contralateral side. In eleven cases with diaphragmatic plateau waves, even the ribs formed plateau-shaped waves on the same side. Of the abdominal cases without definite physical signs, about a sixth had

reduced costal respiration, and about as many showed compensatorily increased costal amplitude. The remainder had an average amplitude. Costal respiration appears to be impaired on the affected side in acute abdominal conditions, but to a lesser degree than diaphragmatic breathing. Restriction of diaphragmatic and costal movements can be explained by reflex defence during painful respiration.

It may be stated that in a preliminary study of kymographic appearances in acute pulmonary conditions, the findings were: Slightly or moderately reduced diaphragmatic amplitude with normal wave form on the affected side. In none of the thoracic cases was a plateau-shaped wave found. A report on the kymographic appearances in thoracic conditions will, it is hoped, follow in due course.

Sources of error. Basal pleural adhesions usually cause restriction of diaphragmatic movements. This must be taken into consideration when examining kymograms, and roentgen examination of the chest should always accompany kymography. Enlargement of the heart may possibly reduce the diaphragmatic amplitude on the left side.

In some patients who underwent kymographic examination a few days after abdominal operation and who obviously had no peritonitis of clinical significance, the diaphragmatic wave was plateau-shaped bilaterally, but the amplitude was only slightly, if at all, reduced. This can be explained by a slight postoperative peritoneal irritation.

In a few non-operated cases a plateau-shaped tracing with normal amplitude was obviously caused by the patients' ignorance of the breathing technique: they held their breath after each expiration. Following instruction and a little practice the same patients produced normal kymograms.

Conclusions

Respiratory kymography makes possible an objective study of the course, amplitude and direction of the diaphragmatic and costal movements.

Considerable restriction of diaphragmatic movements on the affected side, with slight or moderate impairment of costal respiration, is present in practically all the severe abdominal conditions.

Plateau-shaped diaphragmatic waves appear in the more severe cases, most often in inflammatory conditions close to the diaphragm or in organs with intimate connections (lymphatics or loose connective tissue) with the diaphragm. Such a wave indicates peritonitis or peritoneal irritation of a local nature, as in subphrenic abscess or pancreatitis, or general, as in ileus.

Kymographic appearances often make it possible to differentiate abdominal conditions from intrathoracic conditions, and the severe cases from the others. It is possible to localize the process to the right or the left side of the abdomen,

to the gallbladder or the pancreas, for instance. Kymography enables postoperative basal pulmonary complications to be distinguished from subdiaphragmatic conditions.

Respiratory kymography is a simple and rapid examination and causes little or no discomfort to the patient, even if he be gravely ill, and may provide valuable diagnostic information.

SUMMARY

Respiratory kymographic investigations in 87 acute abdominal cases and 30 normal controls are described. The value of recording the diaphragmatic and costal movements in both ordinary and deep respiration is pointed out. A plateau-shaped diaphragmatic wave with reduced amplitude forms a means of estimating the severity of an abdominal process, of its localization, and of differentiating between abdominal and thoracic conditions.

ZUSAMMENFASSUNG

Es werden respiratorische kymographische Untersuchungen an Hand von 87 Fällen von acuten Abdomen und von 30 normalen Kontrollfällen beschrieben. Es wird auf den Wert der Registrierung der Diaphragma- sowie der Rippenbewegungen sowohl bei gewöhnlicher als auch bei tiefer Respiration hingewiesen. Eine plateau-geformte diaphragmale Atemkurve mit reduzierter Amplitude lässt auf die Schwere des abdominellen Prozesses und seine Lokalisation schliessen, und erleichtert die Unterscheidung zwischen abdominalen und thorakalen Affektionen.

RÉSUMÉ

L'auteur présente les résultats d'examens kymographiques respiratoires sur 87 cas d'abdomen aigu et sur 30 sujets témoins normaux. Il souligne l'intérêt de l'enregistrement des mouvements diaphragmatiques et costaux dans la respiration normale et dans la respiration profonde. Une courbe diaphragmatique en plateau avec amplitude réduite permet de juger de la gravité d'un procéssus abdominal, de préciser son siège et de différencier entre affections abdominales et thoraciques.

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MINIATURE SEMICONDUCTOR DOSE RATE METER

by

CARL HELLMUTH HERTZ and ROLF GREMMELMAIER

Great interest has been shown in the last decade in different methods of radiation dose measurements because of the increasing application of roentgen and γ rays in medicine and industry. Dose and dose rate measurements in radiotherapy do not only require a simple and dependable instrument of high sensitivity, and an energy dependence as low as possible, but in many applications it is also of importance that the probe of the meter is as small as possible. There are two reasons for the last requirement: a large dosemeter measures only the mean value of the roentgen beam at the point of interest, and further its size prohibits its introduction into body cavities; such as the oesophagus, for example. Finally, in the case of dose rate meters, a fast response to variations in radiation intensity is desirable.

So far, there is no instrument that fulfills all of these requirements to the desired degree. Therefore the methods used to-day for roentgen measurements more or less compromise between the different demands stated above. For dose measurements the miniature condenser chambers (Bg-chambers) (21) probably conform best with the ideal requirements, although these chambers still have a diameter of 5 mm and a length of 20 mm. The lowest dose that can be detected by them is, however, not less than 1 r. Among other types, the photographic

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film method (1) (4) is energy-dependent, while the use of plastics (14) (2) is possible only for very high roentgen doses. Dosemeters using the photoluminescence or coloration of certain types of glass (8) (12) (13) represent a certain compromise between advantages and disadvantages of these two methods. Finally, even chemical reactions due to radiation have been employed for dose measurements (6).

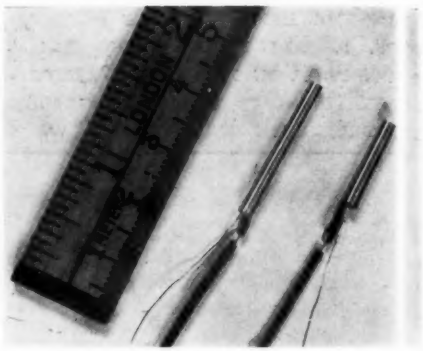

Fig. 1. GaAs semiconductor probes.

For dose rate meters the ionization chamber is probably most commonly in use, in spite of the relatively large chambersize and the high insulation requirements. Smaller probes can be obtained by measuring the conductivity of CdS crystals (17), which is sensitive to ionizing radiation, the drawback being slowness of response and a heavy energy-dependence. Since even the conductivity of polyethylene films have been found to depend on absorbed roentgen intensity, such films have been used for dose measurements in the low energy range (5). Another way to approach the problem is the use of scintillation counters (11) (19) employing probe crystals as nearly tissue-equivalent as possible, but here, except a certain energy-dependence, the transmission of the light from the crystal to the photomultiplier and the relatively complicated electronic equipment may cause difficulties.

If the main requirement in the construction of a dose rate meter is to make the probe element as small as possible, the attention is directed to a further process sensitive to ionizing radiation: the photoeffect in certain semiconductor devices (p-n-junctions). This effect has been investigated by PFISTER (16) for the special case of a GaAs (gallium arsenide) semiconductor, and it was shown that the photocurrent generated in such an element was proportional to the incoming roentgen intensity as long as the inner resistance of the ammeter used was low. Therefore an attempt was made to construct a roentgen dose rate meter using a GaAs p-n-junction.

Probe construction. The obvious reason for the fact that the photoeffect in semiconductors has not been used extensively for roentgen measurement is the high dependence of the photocurrent on photon energy that is to be expected because of the high atomic number of most semiconductors. In the dose rate meter described below this effect is partly counteracted by the special geometry of the probe, thereby making it suitable for roentgen intensity measurements in the conventional roentgen therapy energy range. Further, because of its

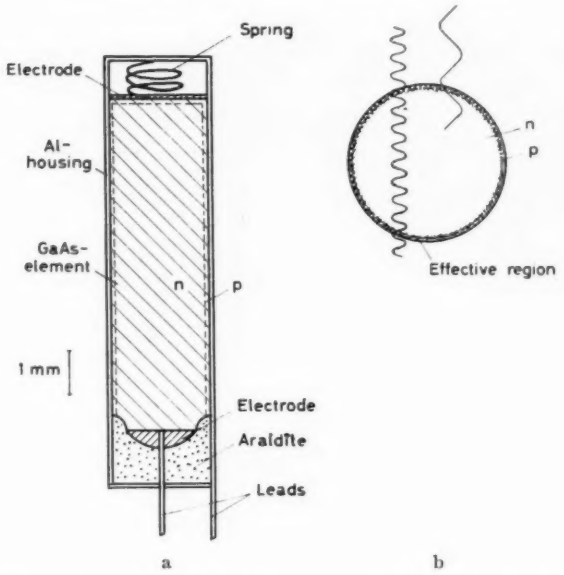

Fig. 2. a) Construction of the roentgen probe. b) Cross section through the probe showing effect of radiation differing in energy. Low energy radiation is absorbed in the probe, while high energy photons transverse it and generate photocurrent on both sides of the probe.

unusually small size, it may even be used in special cases for the measurement of high energy radiation after proper calibration.

Fig. 1 shows the outer appearance of two semiconductor elements while Fig. 2 gives the cross section of such a probe. As shown in the latter figure, it consists of a cylindrical GaAs crystal encased in an aluminium housing, the walls of which have a thickness of 0.2 mm. The GaAs crystal consists of an n-type core and a p-type-layer at the surface, thus containing a p-n-junction about 10 μ below the surface. The p-layer has been produced by diffusing Zn atoms in the n-doped GaAs-cylinder. Electrical contact between the electrode on the p-layer and the aluminium housing is ensured by a spring. One lead is attached to the housing, while the other lead is soldered to the electrode on the core material. The outer diameter of such a probe element is about 2.5 mm and its length between 10 to 25 mm.

For the connection between the probe and the ammeter for measuring the photocurrent a 2 mm thick and very flexible coaxial cable was used. Because of the relatively low impedance of both the probe and the ammeter more than

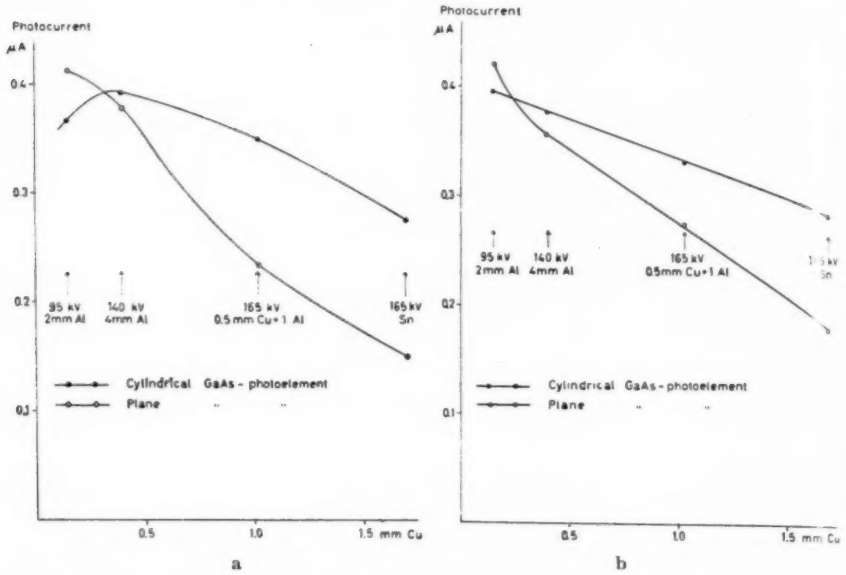

Fig. 3. Photocurrent from a cylindrical and plane semiconductor element at different roentgen qualities at a constant dose rate of 100 r/min. a) On top of a wax phantom. b) Inside the phantom 9 cm below its surface. — Field size 100 cm², FSD 50 cm.

ordinary insulation of this coaxial cable is not required, but it is not advisable to use common wires instead of a coaxial cable, since all AC-signals (alternating current signals) picked up from electric and magnetic strayfields are rectified by the p-n junction and added to the photocurrent.

For the present investigation an electronic ammeter using a chopper amplifier (Siemens Nano-ampèremeter) was used. The instrument had a maximum input impedance of 400 $k\,\Omega$ at its maximum sensitivity of 10^{-9} ampère at full scale deflection. In this connection it is important to use an instrument with an input impedance as low as possible, since only in that case is a linear dependence of the photocurrent on the roentgen intensity and independence from temperature variations ensured (16) (see below).

Properties of the dose rate meter. When the geometry and dimensions of the probe element described above were determined, consideration has been given to the energy-dependence of the photocurrent because of the high atomic number of the semiconductor material. This energy-dependence has been decreased using the following procedure.

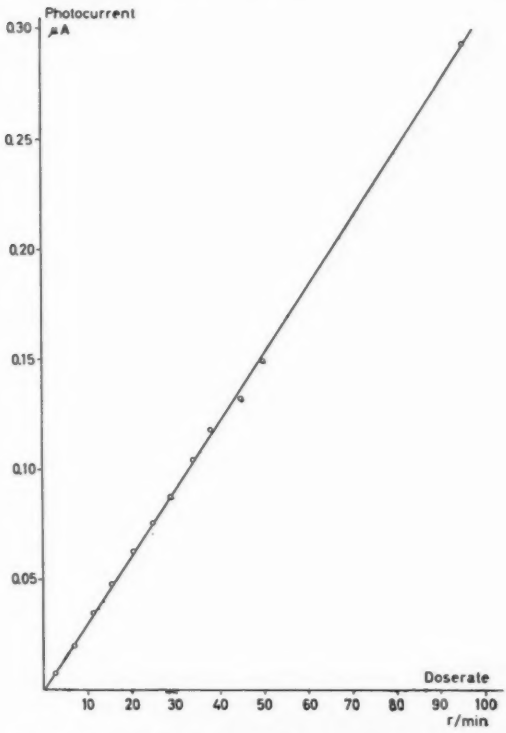

Fig. 4. Linear relation between photocurrent and dose rate. 190 kV, filter 0.5 mm Cu + 1 mm Al, field size 100 cm², FSD 50 cm, 9 cm inside of wax phantom.

The photoeffect in p-n-junctions is due to the fact that the electrons and holes generated in the vicinity of the junction are separated by the inner field of the junction. It is the same process that gives rise to the photocurrent observed in selen photoelements if the latter are exposed to light. For a general discussion of p-n-junctions, see (20) (22). Thus a certain number of low energy photons will generate a higher photocurrent than the same number of high energy quanta, this difference being more and more marked with increasing atomic number of the semiconductor. This energy-dependence is counteracted to some extent by the cylindrical geometry of the probe (Fig. 2b): low energy radiation is absorbed in the probe and generates photocurrent only on one side of it, while roentgen rays of high energy transverse the entire probe, thus transversing the p-n-junction at the front and the backside of the probe. In this way, nearly

two times as much photocurrent is generated by the high energy radiation in the present probe compared with a flat p-n-junction of comparable dimensions and this compensates to some extent for the lower ionization density of the high energy photons.

If this procedure is used, the probe is less energy-dependent than a plane p-n-junction in a certain energy range depending on probe material and diameter. The absorption coefficient of the GaAs semiconductor is very nearly the same as that of germanium, which is about 5 cm^{-1} at a photon energy of 100 keV. Thus a monoenergetic roentgen beam of 100 keV is attenuated to $1/e$ (e = base of natural logarithms) by transversing the probe along a diameter (2 mm), i. e. an energy used in conventional roentgen therapy. We should therefore expect an improvement of its energy-dependence in this energy range.

Fig. 3 shows the energy-dependence of the present probe compared with a plane GaAs element: (a) on the surface of a 18 cm thick wax phantom, and (b) in the wax phantom 9 cm below the surface. The roentgen qualities used are standard in roentgen therapy in Sweden and were generated by a Siemens Reiniger therapy unit (Stabilipan). The actual dose rate was measured by a Philips dose rate meter with a calibrated energy-independent ionization chamber of about 1.5 cm in diameter and 3 cm long, which was placed about 3 cm from the semiconductor probe. The measurements were made at suitable dose rates and then standardized to a dose rate of 100 r/min, which resulted in the values given in Fig. 3. This can be done on account of the linear intensity dependence of the probe (cf. (16) and Fig. 4).

Fig. 3 shows clearly the compensatory effect of the cylindrical probe geometry. Further, in Fig. 3a the probe sensitivity goes through a maximum between half value layers of 0.2 and 0.4 mm Cu, which can be expected from the above considerations. This maximum, which is more accentuated in air, is not due to the 0.2 mm Al housing, since the absorption in the Al wall at the photon energies used here is less than 2 %. The fact that it does not appear in Fig. 3b, where the probe was situated inside the phantom, is due to scattered radiation in the phantom (10). It will be shown below that the effect of this secondary radiation is of great importance for the application of the semiconductor probe to roentgen dosimetry. This restricts the use of the probe to places inside or on the surface of a phantom or patient only.

Fig. 4 shows the dependence of the photocurrent on the dose rate at a roentgen tube voltage of 190 kV. It verifies the linearity of this dependence already found for plane p-n-junctions by PFISTER (16) also for the present probe. As stated above, this linearity is true only if the input impedance of the ammeter is sufficiently low. Since the same is true for the temperature-independence of the probe, an estimation of the magnitude of the maximal permissible input impedance would be of value.

Fig. 5 shows the circuit of the probe arrangement. The photoelement can be represented by a source of the photocurrent I_P, — this current is proportional

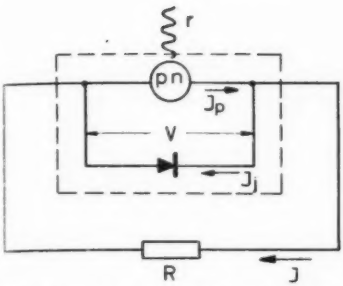

Fig. 5. Electric circuit of semiconductor probe.

to the dose rate and temperature-independent within a wide range — shunted by the internal resistance of the p-n-junction. The external load is the input resistance R of the ammeter. The current I_P flows partly through the ammeter and partly back through the junction itself. Now, the internal resistance of the junction depends on the temperature, the photocurrent, I_P, and the external load, R. Therefore, to get the desired linearity and temperature-independence of the measured current the input resistance of the ammeter should be much lower than the internal resistance of the junction at all dose rates. Then the measured current I is practically equal to photocurrent I_P.

Consideration of the characteristics of the p-n-junction (20) (22) leads to the following two conditions for the input resistance R of the ammeter:

$$R \ll R_o, \tag{1}$$

$$R \ll \frac{kT}{eI_p}; \text{ i. e. } V \ll \frac{kT}{e} \tag{2}$$

R_o being the resistance of the junction at $V = 0$.

This can be shown by using the expression for the current I_j through a p-n-junction (20) (22):

$$I_j = \mathrm{I}_o \left[\exp\left(\frac{eV}{akT}\right) - 1 \right] \tag{3}$$

V being the voltage applied to the junction, a a constant between 1 and 2, k Boltzmann's constant, T the absolute temperature and e the charge of the electron. Thus, for linearity and temperature-independence ($I_j \ll I_p$) we get, using $V = I \cdot R$:

$$I_j = I_o \left[\exp\left(\frac{eIR}{akT}\right) - 1 \right] \ll I_p \tag{4}$$

Using $I \sim I_p$ and $I_p \ll \mathrm{I}_o$, the condition (1) can be derived while $I_p \gg I_o$ gives condition (2).

In our case $R \ll \mathrm{R}_o$, as long as ranges of the ammeter larger than 0.01 μA full scale deflection were used, since at this sensitivity the input resistance was less than 40 $k\Omega$, whereas R_o was found to vary from one probe to another between 10^6 and $10^7\Omega$. Furthermore, the voltage drop at the ammeter was 0.4 mV for full scale deflection in all ranges. This is much less than $\frac{kT}{e}$ at room

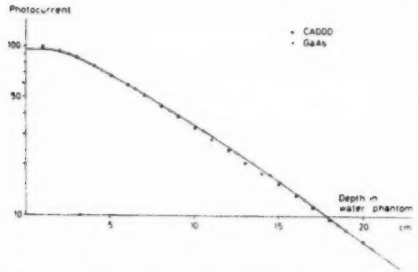

Fig. 6. Photocurrent from semiconductor probe at different depths in water phantom. Current normalized to arbitrary units for comparison with CADDD values. 200 kV, filter 0.5 mm Cu + 1 mm Al. HVL 1.15 mm Cu, field size 100 cm², FSD 50 cm.

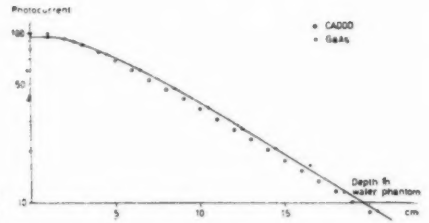

Fig. 7. Comparison between semiconductor probe and CADDD values in water phantom as in fig. 6. Radiation 200 kV, Thoraeus filter, HVL 2 mm Cu, field size 100 cm², FSD 50 cm.

temperature $\left(\frac{k \cdot 300°\ K}{e} \approx 25\ \text{mV}\right)$; so both conditions (1) and (2) were fulfilled. If instead of the photocurrent the photovoltage is measured with a high impedance voltmeter, the photovoltage is not proportional to the roentgen ray intensity, and it is temperature-dependent (15) (16).

Further, it is seen from eq. (4) that if the instrument used for the measurement of the photocurrent has different measuring ranges, changes from one range to another can be made without recalibration of the probe only if $R \ll R_o$. This was the case with the ammeter used in this investigation as long as ranges larger than 0.01 μA full scale deflection were used, since at this sensitivity the input impedance was less than 40 $k\Omega$, while R_o was found to vary from one probe to another between 10^6 and $10^7\Omega$.

In spite of its special geometry the photocurrent of the present probe is shown to be still dependent on the photon energy (Fig. 3). Thus serious difficulties should be expected for its actual application to dose rate measurements in roentgen therapy. Therefore measurements were made in a water phantom using different roentgen qualities, filters and field sizes. Each time the dose distribution along the central axis of the beam was measured and compared with the values given by CADDD tables (3). Some of the results are shown in Figs 6 and 7. In these figures the line represents the photocurrent measured from different depths of the probe in the water tank while the circles are values given by the CADDD tables. In these figures the photocurrent has been normalized in such a way that both curves coincide at a water depth of 2.5 cm. This was necessary since it was difficult to place the semiconductor probe exactly on the surface of the water phantom used.

Fig. 6 shows the thus normalized photocurrent as a function of the depth in the water phantom using a voltage of 200 kV at the roentgen tube, 0.5 mm

Cu + 1 mm Al filter, field size 100 cm², FSD 50 cm. The HVL of the radiation was 1.15 mm Cu. As shown by the figure, the maximum deviations are less than 3 %. Fig. 7 shows the results obtained with a more energetic radiation, the HVL of which was 2 mm Cu (tube voltage 200 kV, Thoraeus filter, field size 100 cm², FSD 50 cm). In this case the largest deviations of all the measurements made were observed: the maximum deviation being 10 %. Except for these two examples a tube voltage of 175 kV was used with the filters 0.2 mm Cu + 1 mm Al, and 0.5 mm Cu + 1 mm Al (HVL 0.54 mm Cu and 0.95 mm Cu, respectively) where maximum deviations of 5 % were observed. Further, using a tube voltage of 200 kV and a 0.5 mm Cu + 1 mm Al filter, field sizes of 20 and 10 cm² were investigated. Using a field size of 20 cm², the deviations were less than 4 % while with a field size of 10 cm² the deviations at a water depth of more than 12 cm increased up to 10 %, probably due to insufficient adjustment of the probe position since at this field size the length of the probe used was nearly as large as the field dimensions. Square fields and FSD of 50 cm were used throughout the investigation.

Because of the relatively large energy-dependence of the probe the surprisingly good agreement between the CADDD values and the semiconductor probe cannot be understood immediately. The reason for this must be sought in the effect of the scattered radiation induced in the water phantom by the primary beam. This scattered radiation was recently investigated by HETTINGER, LIDÉN and STARFELT (9) (10), who showed a marked shift in the photon energy of the scattered radiation to longer wavelengths. From these papers it can be seen that the spectra of the scattered radiation in different directions does not change appreciably with the depth in the water phantom, which is even more valid for the HVL of the secondary radiation (9, Table VI). This seems to be even more true with decreasing field size. Thus, if the photocurrent generated in the semiconductor probe is to a large extent due to the scattered radiation, no great differences between the CADDD values and the present probe can be expected. The increasing accuracy of the probe with smaller field sizes, and the fact that the secondary radiation consists to a larger extent of photons with energies around 100 keV, i. e. photon energies for which the probe is most sensitive (Fig. 3) seem to support this assumption. Further, since the semiconductor probe is nearly energy-independent in the energy range around 100 keV because of its geometry, it can easily be explained that small changes in the scattered radiation spectra due to different depths in the phantom do not influence the photocurrent noticeably.

The dependence of the photocurrent on the angle of incidence of the roentgen beam is also influenced strongly by the secondary radiation generated in the phantom. Fig. 8 shows this relation: with the probe placed in the middle of a cylindrical wax phantom (diameter 25 cm) (Fig. 8a) and in air (Fig. 8b). Two radiation qualities were used in both cases: 95 kV, filter 2 mm Al (HVL 0.14 mm Cu) and 200 kV, filter 0.5 mm Cu + 1 mm Al (HVL 1.15 mm

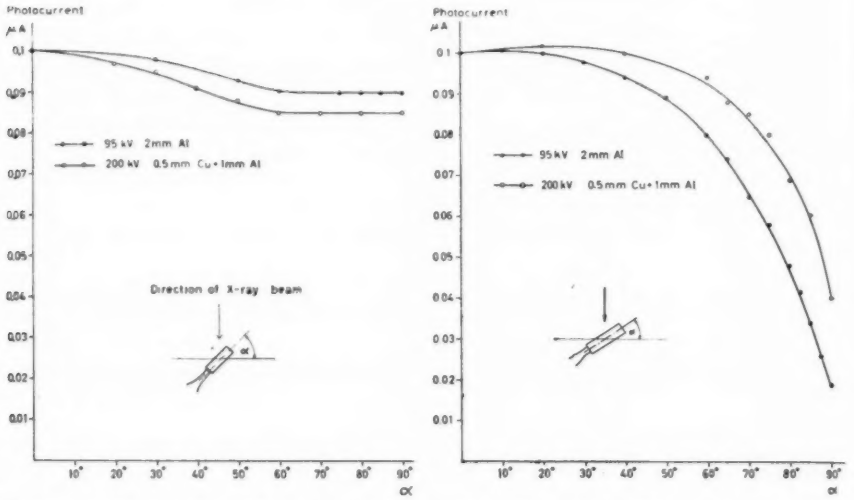

Fig. 8. Angular dependence of photocurrent for two different roentgen qualities: inside a cylindrical wax phantom (left diagram) and in air (right diagram).

Cu). It is clearly shown by these diagrams that the photocurrent depends much less on the angle of incidence if the probe is placed in the phantom (Fig. 8a). Even this behaviour can be explained by secondary radiation to the generation of the photocurrent in the p-n-layer. Obviously the relatively small dependence of the photocurrent on the angle of incidence is of importance for the actual application of the semiconductor probe in roentgen therapy, since small deviations from vertical incidence are unavoidable during the treatment of the patient. However, it should be kept in mind that this is true only if the probe is situated inside the patient.

In the energy range investigated above the probe has a sensitivity of about 3.10^{-7} ampère per 100 r/min (Fig. 4), but this sensitivity differs from probe to probe due to differences in the manufacturing process of the p-n-junction. Thus among nine semiconductor probes of the same geometric dimensions investigated in this paper two were shown to have a sensitivity of only one-fourth of the above-named value, while others lay in between these extremes. In spite of this, their relative energy-dependence and other behaviour were exactly the same. Since the geometry of the probes is identical, the reason for the difference in the sensitivity must be due to differences of the diffusion length of electrons and holes in the vicinity of the p-n-junction (7). Measurements of this effective layer in the above-named probes with the method by GREMMELMAIER (7) agree with the sensitivities found, as shown by the Table on p. 79.

Table

robe No.:	1	2	3	4	5	6	7	8	9
ensitivity (μA/100r/min)	20	18.5	11.5	11.5	7.0	30	16	7	8.6
hickness of effective layer (μ)	4.5	4.5	2.3	1.7	1.7	6.1	3.5	1.4	1.7

All the probes, except No. 4, show good proportionality between the thickness of the effective layer and the sensitivity. Since the depth of the p-n-junction under the surface of the material is estimated to be about 10 μ, the effective layer does not reach the surface. Thus it seems to be certain that while each probe has its own sensitivity, the characteristics of the probes with regard to photon energy and angle of incidence etc are the same. Further, it has been shown that the sensitivities of the probes did not change for a whole year, during which they were only sporadically exposed to roentgen rays. Other investigations (18) showed that even very high doses of conventional roentgen therapy did not change the sensitivity of p-n-junctions in semiconductors. Thus for calibration of a probe it is only necessary to determine its sensitivity at one quality of roentgen rays.

Because of the inherent properties of the photoeffect in the p-n-junction, and the low impedance of the measuring circuit, the time of response of the dose rate meter is very small. At present, this time constant is determined by the time necessary for electrons and holes to leave traps in the semiconductor and has been found to be about 2.10^{-3} sec (16). Since the time of response of the ammeter is much greater (about 0.5 sec), the response time of the present dose rate meter is only limited by the ammeter.

SUMMARY

A small dose rate meter has been constructed for measurements inside body cavities using the photoeffect in a p-n-junction of a GaAs semiconductor. Because of the special geometry of the probe element its energy-dependence in the conventional roentgen therapy range is reduced and shown to be quite satisfactory inside a water phantom. The length of the cylindrical probe is 10 to 25 mm, its diameter 2.5 mm and its sensitivity about 3.10^{-9} A per r/min.

ZUSAMMENFASSUNG

Ein kleines Halbleiterelement zur Messung der Röntgendosisleistung in Körperhöhlen wird beschrieben. Es benutzt den Photoeffekt in dem p-n-Übergang eines GaAs-Halbleiters. Die Wellenlängenabhängigkeit des Elementes wird durch seine spezielle Geometrie innerhalb des konventionellen Röntgentherapiebereiches weitgehend kompensiert, was durch Messungen im Wasserphantom bestätigt wird. Die Länge des zylinderförmigen Elementes ist 10 bis 25 mm, sein Durchmesser 2.5 mm und seine Empfindlichkeit ca 3.10^{-9} A pro r/min.

RÉSUMÉ

Un débimètre, de faible encombrement, a été construit pour effectuer des mesures à l'in térieur du corps humain. Cet appareil utilise l'effet photoélectrique dans une jonction p- d'un semi-conducteur GaAs. Grâce à la forme géométrique de la sonde, la réponse en fonc tion de l'énergie des photons incidents, dans le domaine de la radiothérapie conventionnell est assez satisfaisante à l'intérieur d'un fantôme d'eau. La longueur de la sonde est de 10 25 mm, son diamètre de 2.5 mm. La sensibilité de l'appareil est d'environ 3.10^{-9} A par r/mi

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